ANNALS OF SURGERY

VOL. 113 APRIL, 1941 No. 4

ENDEMIC GOITER IN JAPAN*

KUNIO KAWAISHI, M.D.

AND

YOSHIO HASHIMOTO, M.D.

TAIHOKU, FORMOSA, JAPAN

FROM THE DEPARTMENT OF SURGERY, TAIHOKU IMPERIAL UNIVERSITY, TAIHOKU, FORMOSA, JAPAN

IT is well known that goiters are unusual in Japan and it is commonly believed that there are no endemic goiter regions such as are present in Switzerland. Dr. E. Papellier,[1] who has resided in Japan for 50 years, reported, in 1938, on the occurrence of goiters in Japan, and attributed the scarcity of the disease to the high iodine content of the diet in which sea-weeds are constantly used.

Dr. J. F. McClendon,[2] who resided in Japan for one year, as exchange professor, described the mountainous districts of Honshu (main island) and Hokkaido, Japan, as the goitrous areas, in 1935. But his so-called goitrous area is such that only five goiters were found among a population of 2,500. Formosa, which he described as a nongoitrous area, is, in fact, the only real endemic goitrous area in Japan.

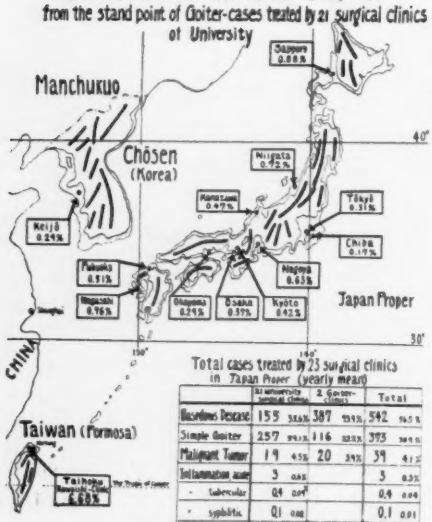
A. DISTRIBUTION OF GOITER IN JAPAN PROPER.—In order to get some idea of the relative distribution of goiter in Japan, the authors have inquired and received information from 21 University Surgical Clinics, and from two Goiter Clinics of our country, in regard to the goiters treated during the last five years. Table I represents the distribution of goiters as obtained from the above information. As shown in the map, 0.17 to 0.88 per cent of all surgical cases in the University Clinics are goiters, and there is little difference among the various parts of Japan. The total number of goiters operated upon yearly in the 21 University Surgical Clinics does not exceed 435 cases, and likewise in the two Goiter Clinics it does not exceed 523 cases. The total of these clinics is 958 cases, out of which 38.9 per cent are simple goiters and 56.5 per cent are Basedow's disease and hyperthyrosis. In the Goiter Clinics, Basedow's disease and hyperthyrosis predominate and only 22.2 per cent are simple goiters.

* Read before the Third Pan-Pacific Surgical Congress, September 21, 1939, at Honolulu, Hawaii. Submitted for publication October 18, 1939.

TABLE I

Distribution of Goiter in Japan

from the stand point of Goiter-cases treated by 21 surgical clinics of University



Total cases treated by 23 surgical clinics in Japan Proper (yearly mean)

	21 university surgical clinics		2 Goiter-clinics		Total	
Basedows Disease	155	32.6%	387	93.5%	542	56.5%
Simple Goiter	257	54.1%	116	28.0%	373	38.9%
Malignant Tumor	19	4.0%	20	4.8%	39	4.1%
Inflammation acute	3	0.6%			3	0.3%
" tuberculer	0.4	0.08%			0.4	0.04%
" syphilitic	0.1	0.02%			0.1	0.01%
Total	434.5	100%	523.0	100%	957.5	100%

TABLE II

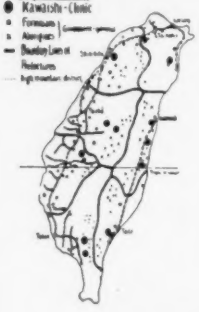
The Materials on which this Report is based.

	Number Examined	Number of Goiter	Rate of Affection in % Total	Male	Female	♂ : ♀
The examination at Kawaishi-Clinic (in 12 neighbouring Prefectures)	56082	19742	35.2%	26.1%	44.9%	1 : 1.7
in out patients at 3 years duration	1989	183	6.6%	0.8%	13.4%	1 : 16.9
Total	58071	19925	34.3%	25.2%	43.9%	1 : 1.7
The examination at the government-general Formosa-area	193716	5340	2.8%	0.8%	4.9%	1 : 5.8
Aborigines	65917	1465	2.2%	0.8%	3.6%	1 : 4.5
Simple Goiters treated by 21 university Hospitals and 2 Goiter-Clinics of Japan Proper (yearly mean)		375	0.4%	0.14%	0.62%	1 : 4.4

Regions of Examination.

Explanations

- Kawaishi-Clinic
- Formosans
- Aborigines
- Boundary Lines of Prefectures
- high mountain district



The Cases operated during the last one year in Kawaishi-Clinic.

	Race	Total	Male	Female
Endemic Goiter	Japanese (Settlers)	8	1	7
	Formosans	23	2	21
	Aborigines	39	4	35
	Total	70	7	63
Basedows disease	Japanese (Settlers)	5		5
	Formosans	4	2	2
	Aborigines	0		
	Total	9	2	7
Cancer	Formosans	1	1	
	Aborigines	1		1
Cretin	Formosans	1		1
Total		82	10	92

TABLE III

Results of Examination in endemic Regions.

1568 Goiters out of 49011 Persons. Rate: 31.9 %

Race	Region	Examined Persons	Goiter	Rate of Affektion % Total	♂	♀	♂ : ♀
Japanese Settlers	Shirakawa (Karenkō)	45	10	22.2%	19.0%	25.0%	1 : 1.3
	Yoshino (")	966	131	13.5%	10.2%	16.0%	1 : 1.5
	Kamiyamato (")	165	13	7.8%	4.0%	13.6%	1 : 3.4
	Ōka (Taihoku)	73	4	5.4%	0.	12.5%	
	Turin (")	178	1	0.5%	0.	1.1%	
	Total	1427	159	11.1%	7.6%	14.2%	1 : 1.8
Formosans.	Rokka (Shinchiku)	8111	3862	47.6%	31.5%	63.7%	1 : 2.0
	Mori (Taichū)	892	358	40.1%	27.3%	52.7%	1 : 1.9
	Ōka (Taihoku)	25212	6200	26.7%	18.8%	35.3%	1 : 1.8
	Sansei (")	1107	245	22.1%	11.2%	32.9%	1 : 2.9
	Koume (Tainan)	1784	362	20.6%	10.1%	27.1%	1 : 2.6
	Pinam (Taito)	1768	288	16.2%	10.3%	23.6%	1 : 2.2
	Mōrin (Karenkō)	230	32	13.9%	7.2%	23.6%	1 : 3.2
	Total	37104	11347	30.5%	20.6%	41.2%	1 : 2.0
Aborigines.	Mizuho (Karenkō) Am	1722	1093	63.5%	44.8%	78.8%	1 : 1.7
	Mōrin (") "	4184	2238	53.5%	31.8%	71.8%	1 : 2.2
	Kantabar (Taichu) Bunun	104	47	45.2%	?	44.6%	
	Bainam (Taito) Bunun	368	120	32.6%	21.4%	42.0%	1 : 1.9
	Rai (Takao) "	691	135	19.5%	16.1%	23.1%	1 : 1.4
	Tokoyanya (") "	1176	198	16.8%	12.2%	21.6%	1 : 1.7
	Pinam (Taito) "	1223	330	27.1%	11.5%	21.8%	1 : 1.8
	Pinam (") Ami	88	4	4.5%	4.8%	4.2%	1 : 0.8
	Mizuho (Karenkō) Bunun	222	10	4.5%	2.7%	6.1%	1 : 2.2
	Total	10480	4175	39.8%	25.4%	52.2%	1 : 2.0

TABLE III

Results of Examination in Primary School and Public School.

4111 Goiters out of 7071 Pupils. Rate: 58.1%

Race	School.	Number of Pupils	Goiters	Rate of Affection in % Total.	♂	♀	♂ : ♀
Japanese Settlers	Kamiyamato Primary School (Karenkō)	112	41	36.6%	30.1%	44.8%	1 : 1.4
	Yoshino "	313	86	27.4%	21.6%	32.7%	1 : 1.5
	Total	425	127	29.8%	24.1%	35.5%	1 : 1.4
Formosans.	Rokka Public School (Shinchiku)	692	571	82.5%	80.8%	87.2%	1 : 1.1
	Shirakawa " (Karenkō)	356	275	81.8%	79.2%	88.4%	1 : 1.1
	Kan-en " (Taihoku)	462	328	70.9%	69.4%	75.8%	1 : 1.1
	Rika " (Taitō)	36	25	69.4%	70.0%	68.7%	1 : 0.9
	Turin " (Taihoku)	1255	799	63.6%	57.8%	71.3%	1 : 1.2
	Chippon " (Taitō)	115	69	60.0%	52.3%	69.2%	1 : 1.5
	Mōzan " (Shinchiku)	69	36	52.1%	41.6%	76.1%	1 : 1.8
	Tomida " (Karenkō)	107	53	49.5%	38.7%	64.4%	1 : 1.6
	Taiko " (Taihoku)	217	102	47.0%	44.6%	50.0%	1 : 1.1
	Senzan " (")	1248	551	44.1%	42.5%	46.3%	1 : 1.1
	Kamiyamato " (Karenkō)	219	88	40.1%	36.0%	46.9%	1 : 1.3
	Total	4757	2896	60.8%	58.3%	64.8%	1 : 1.1
Aborigines.	Shirakawa Public School (Karenkō)	189	184	97.3%	97.5%	97.0%	1 : 1.0
	Kamiyamato "	296	225	76.0%	71.8%	80.8%	1 : 1.1
	Tomida "	496	313	63.1%	50.1%	76.5%	1 : 1.5
	Rika " (Taitō)	62	37	59.6%	55.2%	66.6%	1 : 1.2
	Chippon "	80	47	58.7%	54.5%	63.8%	1 : 1.1
	Nōkō " (Taichū)	144	83	57.6%	48.0%	52.0%	1 : 1.1
	Makazayazaya " (Takao)	258	103	39.9%	33.6%	47.4%	1 : 1.4
	Rai "	190	65	34.2%	37.5%	30.9%	1 : 0.8
	Mahoan " (Karenkō)	174	31	17.8%	13.4%	21.7%	1 : 1.6
	Total	1289	1088	57.5%	535%	624%	1 : 1.1

Dr. Y. Okano,[5] of the Kyoto Imperial University Hospital, reported 283 goiter cases from various Medical, Pediatric, Surgical, and Gynecologic Clinics, and showed the same relation in which Basedow's disease and hyperthyrosis correspond to 53.4 per cent of all goiters. In other words, it is evident that Basedow's disease and hyperthyrosis are prevalent in Japan proper, and simple goiters are seen only sporadically. This finding corresponds to the situation in Hamburg, Germany, where hyperthyreoses are found

TABLE V

The Geographical Distribution of Goiters.

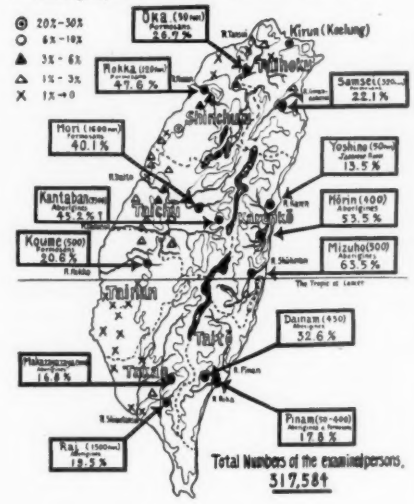


TABLE VI

Per Cent Affected Among Races.

School children.

Region	Japanese Proper	Formosans	Aborigines
Kamiyamato School	36.6%	40.1%	76.0%
Tomida ·		49.5%	63.1%
Shirakawa ·		81.8%	97.3%
Rika ·		69.4%	59.6%
Chippon ·		60.0%	58.7%

Non School children.

Region.	Japanese Proper	Formosans	Aborigines
Shirakawa	22.2%		63.5%
Kamiyamato.	7.8%	13.9%	53.5%
ŌKa	5.4%	26.7%	
Pinam		16.2%	17.1%

in 50 per cent of all goiters. As in the other countries, hyperplastic thyroids at puberty are seen generally in Japan.

During the past one and one-half years our clinic has surveyed the endemic goiter in Formosa, which, at this time, we wish to report in full.

B. Endemic Goiter in Formosa.—(1) *Material Considered* (Tables I, II, III and IV).—This report is based on 19,925 goiters examined at our Out-Patient Clinic and also observed during the survey conducted by us in the 13 endemic regions. In addition, it is based on 6,955 goiters which had been reported ten years before by the governor general of Formosa from a survey of all native and 54 Formosan villages. According to our survey, the disease rate is 44.9 per cent, a rather high rate, because the investigation was conducted only in the highly endemic regions. On the other hand, the reported rate of the government survey is 2.2 to 2.8 per cent. This low rate may be accounted for by the fact that: (1) The survey was conducted either in the nonendemic regions; or (2) slight swellings of thyroids in children were overlooked. Hence, if the survey had been properly carried out, the rate should have been three times as high.

(2) *Geographic Distribution* (Table V).—Primarily, it is essential to

describe the geographic features and climate of Formosa. Formosa extends both into the tropical and subtropical zones, with the tropic of Cancer passing through its center. The greater portion of the island is mountainous, and it is a trifle smaller than Switzerland. A mountain range, occupying the middle of the island, extends from north to south, thus dividing the island into an eastern and western portion. Furthermore, there is a small sea coast range running parallel to the former in the eastern part of the island. The former range has a very high altitude and is formed by 48 mountain peaks of over 10,000 feet, the highest being 13,000 feet.

The Japanese proper and the Formosans live on the plains, while the Aborigines live mostly in the mountainous districts. Goiters are found all over the island but are, however, more prevalent in the subtropical, northern section than the tropical, southern section. The highest rate of incidence (Tables II, III and IV) is 63.5 per cent of the total population, out of which, 78.8 per cent, are found in the female, when only the female population is considered (Shirakawa of Mizuho). There are five endemic regions with disease rates of over 40 per cent; one with 32.6 per cent; three with 20 to 30 per cent; and four with 10 to 20 per cent.

Goiters are prevalent in the regions of the foothills in general, while along the seacoast they are very infrequent. The highly endemic regions, such as Shirakawa of Mizuho (Aborigines 63.5 per cent), Kamiyamato and Tomida of Hōrin (Aborigines 53.5 per cent), Oka (Formosans 26.7 per cent), Rokka (Formosans 47.6 per cent), Kokkan (26.2 per cent), Koume (Formosans 20.6 per cent), Sansei (Formosans 22.1 per cent), *etc.*, are located at the foot of the mountains, situated at 50 to 750 feet above sea level. Hori, the highest Formosan village, situated at 1,600 feet above sea level, has a very high rate of 41.1 per cent.

In the mountainous districts above 3,700 to 4,000 feet above sea level, where the Aborigines reside, many goiters are found. This fact indicates that the height of the village has no relation to the endemic nature of goiter. Furthermore, the type of goiter is not influenced by the height. The so-called "mountain-goiters," or multiple nodular goiters, are seen not only in the mountainous regions but also in places of low elevations of 50 to 500 feet, namely, Mizuho, Horin, Oka, *etc.* In one village the diffuse type may be prevalent, while in the others the nodular type may be more common. The different types of goiter depend rather on the district, race, and food, to which we shall refer later on.

(3) *Incidence Rate in Different Races* (Table VI).—There are different tendencies in respect to the affection among the three races in Formosa. The Japanese proper are less involved; the Formosans come second, and the Aborigines are highly susceptible. The percentages of incidence in each race, in the six most populated endemic regions, are 18.0, 44.7 and 61.1 per cent, namely, 1 :2 and 5 :3.5. This difference is due to the diet and mode of life of these different races. For example, the Japanese proper use seafoods in great quantity in the diet while the others rarely use them.

TABLE VII

Ratio of goitrous female to male in age.

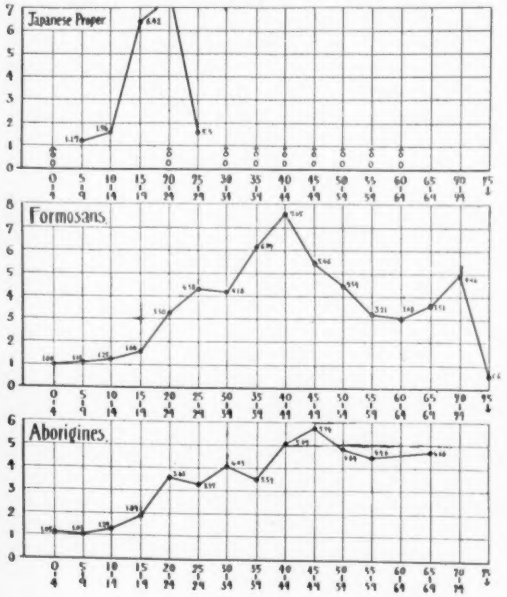


TABLE VIII

Per Cent of Affection According to Age.

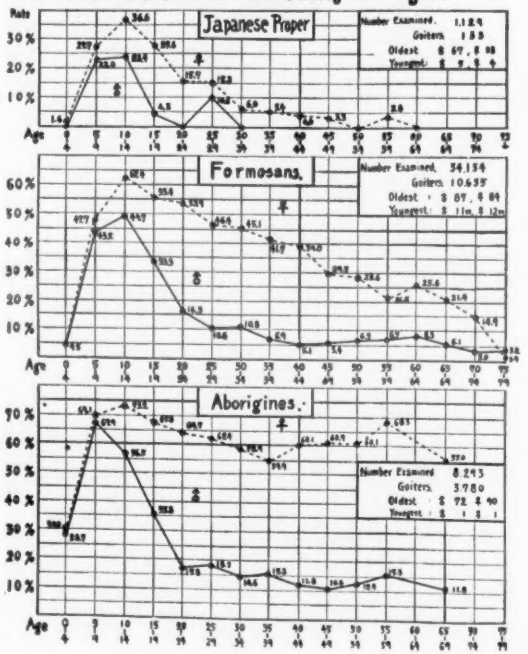
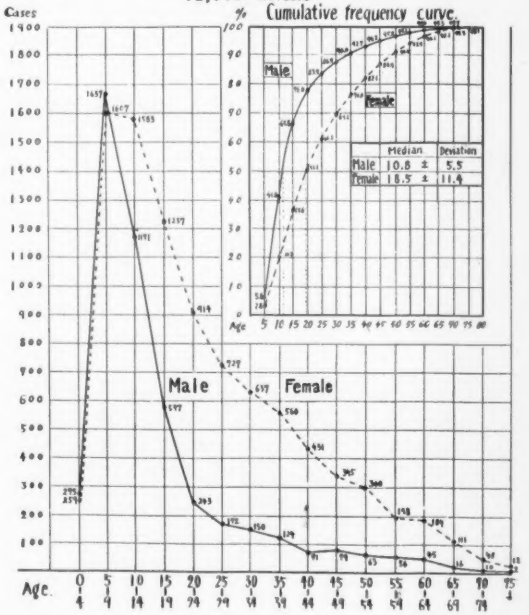


TABLE IX

Number of Goiters According to Age.

13,866 Goiters.



Among the nine native tribes, different disease rates are found. The Ami, who live in the plains of the eastern part, show the highest rate of affection, namely, 63.5 per cent (Shirakawa and Turuoka of Mizuho) and 53.5 per cent (Kamiyamato and Tomida of Horin). The Bunun and the Zuo, who

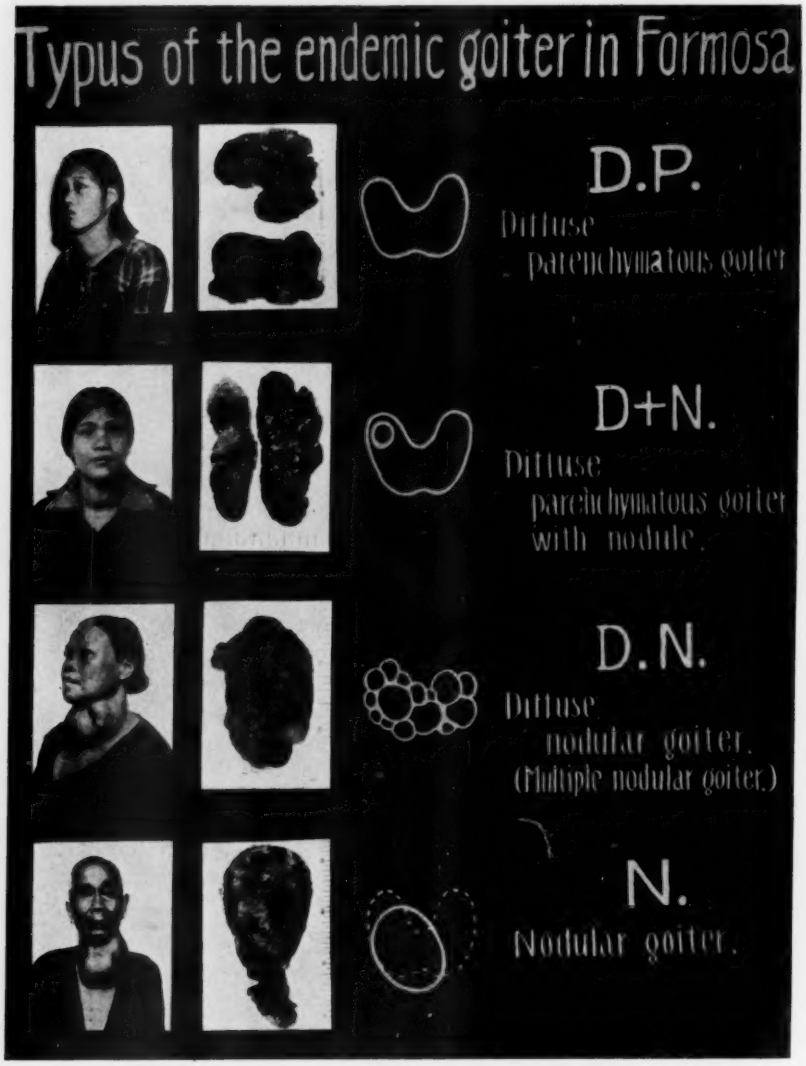


PLATE I.—Showing the types of endemic goiter in Formosa.

live in the mountains, come second. There is little or no difference among the other tribes that live in the mountains.

The type of goiter also differs among the different races, the nodular type being more common among the Aborigines, while the diffuse type is more prevalent among the Formosans.

(4) *Relation of Goiter to Sex* (Tables III, IV and VII).—As in the other countries, goiter affects the female more than the male. The female to male ratio is between 1:45 in Formosa. The rate of incidence in the different sexes depends on the endemicity of goiter and age. The higher the endemicity, the greater the proportion of males affected. The seacoast districts have the lowest ratio because of their low endemicity. The ratio varies with age (Table VII); in childhood, this ratio is low, but it increases with age, because the females are affected in larger numbers. It reaches its maximum of 5.7 per cent (Aborigines) and 7.7 per cent (Formosans) at 40 to 50 years of age, after which it decreases.

(5) *Relation Between Age and Goiter* (Tables VII, VIII and IX).—Goiters are found among all ages in the endemic regions, and have been observed in an 11-month-old infant, to a 90-year-old female. Congenital goiter has never been seen in Formosa.

Table VIII represents the rate of incidence in each five-year period of 14,548 cases observed among a population of 43,576. The highest percentage of goiters is found in the prepuberty period of ten to 14 years. It decreases very gradually in the female, but in the male it decreases very rapidly until 20 to 25 years of age. After that, both sexes show almost the same rate of decrease. Such decrease in the rate after puberty depends on the endemicity —the lower the endemicity, the more rapid the decrease. The highest incidence of goiter is in the puberty period of 14 to 20 years—which corresponds to the universal, true incidence of goiter throughout the world. The difference of race has no effect whatsoever.

C. Clinical Classification.—(1) *Morphologic Classification and Course of Development*: From our survey of 14,345 cases, we prefer to classify the endemic goiter of Formosa into the following four types (Plate I): (1) Diffuse parenchymatous goiter (DP). (2) Diffuse parenchymatous goiter with nodules (DN). (3) Nodular goiter (N). (4) Diffuse nodular goiter (DN). Each type is represented in Plate I. Under parenchymatous goiter, the colloid and the follicular types are included, since they are often difficult to differentiate clinically. Table X represents the classification of each type. The majority, or 80.9 per cent, belong to the diffuse parenchymatous type. The nodular type, both single or multiple, is represented by 19.1 per cent. The distribution of each type depends upon the age and race. The nodular type is found in 41.6 per cent of the goiters among the Aborigines, 11.3 per cent of those of the Formosans, and in 2.1 per cent of those of the Japanese. The parenchymatous goiter is unusual among the adults of the Japanese proper and the Aborigines, but is numerous among the Formosans.

The age distribution of each type is represented in Tables XI and XII; the race distribution is also shown in Table X. The diffuse parenchymatous goiter reaches its greatest incidence at 12 years of age and then rapidly decreases. On the other hand, nodular goiter increases with age (Table XI). The former may be designated as the goiter of childhood and young people, and the latter the goiter of middle life and older people.

The following conclusions have been reached in regard to the development of each type: Endemic goiters develop mostly as the diffuse parenchymatous type and may remain as such or may progress into the diffuse parenchymatous goiter with nodule and may further develop into diffuse nodular goiter. It may develop, on the other hand, as a nodular type from the beginning and

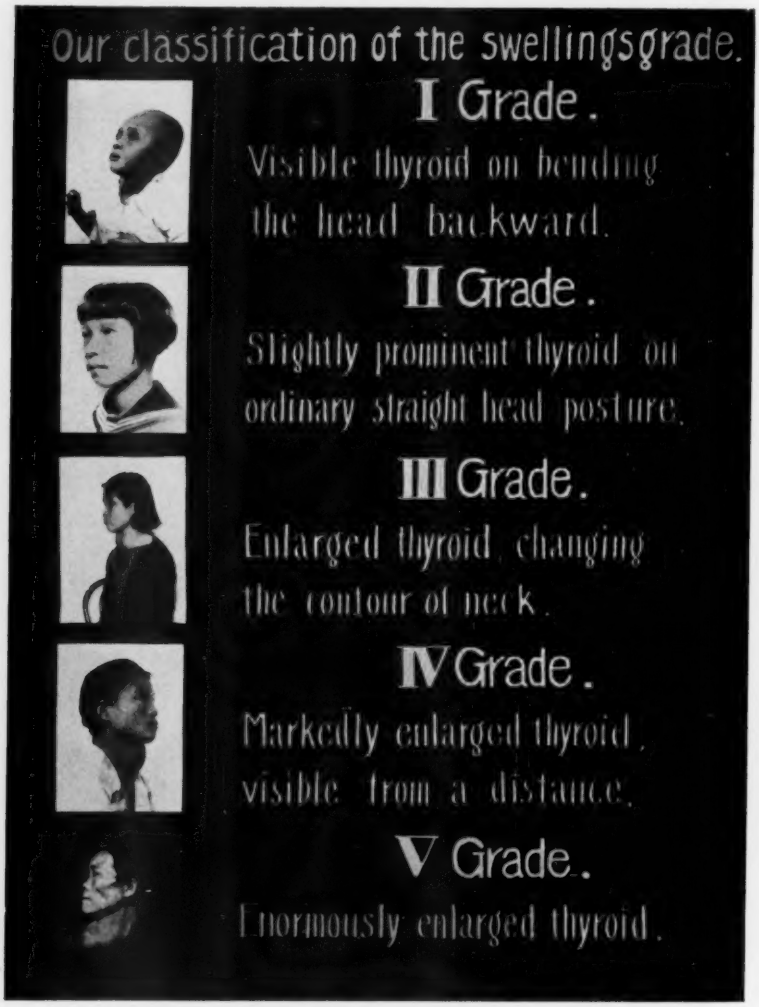

Our classification of the swellingsgrade.
I Grade.
Visible thyroid on bending the head backward.
II Grade.
Slightly prominent thyroid on ordinary straight head posture.
III Grade.
Enlarged thyroid changing the contour of neck.
IV Grade.
Markedly enlarged thyroid, visible from a distance.
V Grade.
Enormously enlarged thyroid.

PLATE II.—Showing the authors' classification into grades according to the degrees of swelling of the thyroid gland.

remain as such and enlarge or transform into a diffuse nodular goiter (Table XIII). Therefore, larger goiters are much more common in the older people, and usually the nodular or diffuse nodular types are the more prevalent.

Size (Plate II).—We have classified the different goiters into five grades according to the modified scale of Dieterle. The grades of swelling are related

TABLE X

Classification According to Types.

Number of Goiters. 14345.

Race	Sex	D. P.		D + N		D.N.		N.		Total	
Japanese Proper.	♂	45	97.8%					1	2.2%	46	100%
	♀	45	97.9%					2	2.1%	97	"
	Total	140	97.9%					3	2.1%	143	"
Formosans.	♂	3288	91.5%	96	2.1%	30	0.8%	199	5.5%	3593	"
	♀	7985	87.3%	309	4.5%	132	1.9%	424	6.1%	6850	"
	Total	9273	88.7%	385	3.6%	162	1.5%	623	5.9%	10443	"
Aborigines.	♂	802	73.9%	57	5.2%	6	0.5%	219	20.2%	1084	"
	♀	1394	52.1%	413	15.4%	109	4.0%	759	28.3%	2675	"
	Total	2196	58.4%	470	12.5%	115	3.0%	978	26.0%	3759	"
Total.	♂	4135	87.5%	153	2.8%	36	0.7%	419	8.8%	4723	"
	♀	7974	77.6%	722	7.5%	241	2.5%	1185	12.3%	9622	"
	Total	11609	80.9%	855	5.9%	277	1.9%	1604	11.1%	14345	"

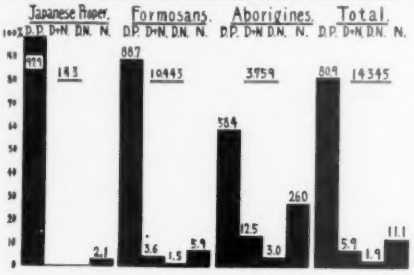


TABLE XI

Distribution According to Age of Each Type.

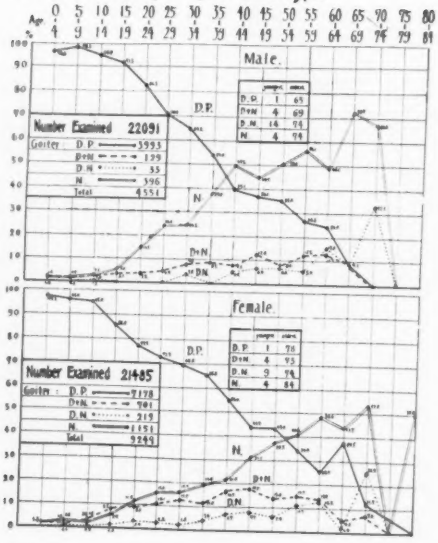


TABLE XII

Number of Goiter-types According to Age.

13,866 Goiters.

Types \ Age	0—10	10—10	20—10	30—10	40—10	50—10
Diffus goiter	80.9%	79.7%	60.9%	51.5%	39.8%	32.7%
Nodular goiter	19.1%	25.3%	39.6%	48.7%	60.2%	67.3%

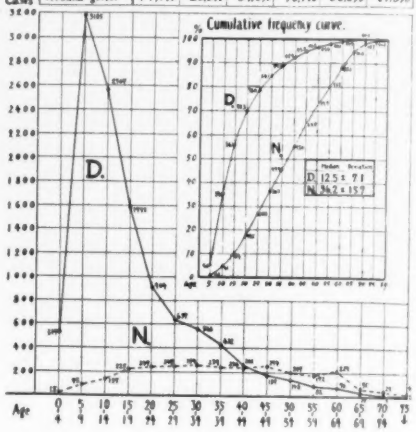


TABLE XIII

Development of the endemic goiter.

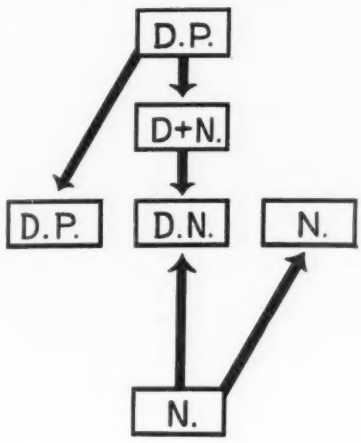


TABLE XIV

Classification Based on Swelling.

Number of Goiters: 14,683.

Race	Sex	I.		II.		III.		IV.		V.		Total	
Japanese Proper.	♂	42	91.3%	3	6.5%			1	2.2%			46	100%
	♀	79	81.4%	17	17.5%			1	1.1%			97	"
	Total	121	84.6%	20	13.9%			2	1.5%			143	"
Formosans.	♂	3046	80.2%	648	17.0%	88	2.3%	9	0.2%	3	0.1%	3794	"
	♀	4331	62.4%	2037	29.3%	472	6.8%	65	0.9%	31	0.4%	6936	"
	Total	7377	68.7%	2685	25.0%	560	5.2%	74	0.6%	34	0.3%	10730	"
Aborigines.	♂	781	70.3%	261	23.5%	46	4.1%	16	1.4%	6	0.5%	1110	"
	♀	1179	43.6%	907	33.5%	394	14.5%	154	5.7%	66	2.4%	2700	"
	Total	1960	51.4%	1168	30.6%	440	11.5%	170	4.4%	72	1.8%	3810	"
Total.	♂	3869	78.1%	912	18.4%	134	2.7%	26	0.5%	9	0.1%	4950	"
	♀	5589	57.4%	3051	31.3%	866	8.8%	220	2.2%	97	0.9%	9733	"
	Total	9458	64.4%	3873	26.9%	1000	6.8%	246	1.6%	106	0.7%	14683	"

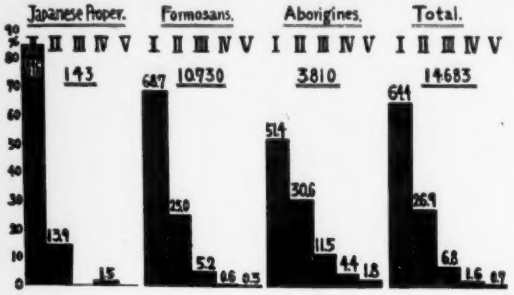


TABLE XV

Number of Goiters According to the Different Grades of Swelling and its Distribution as to Age.

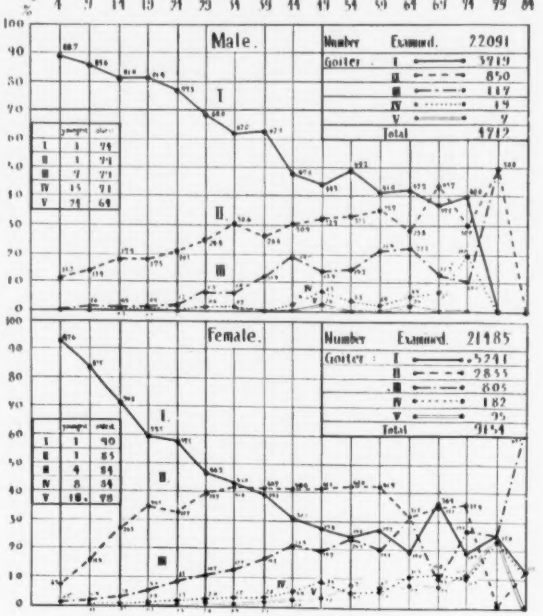
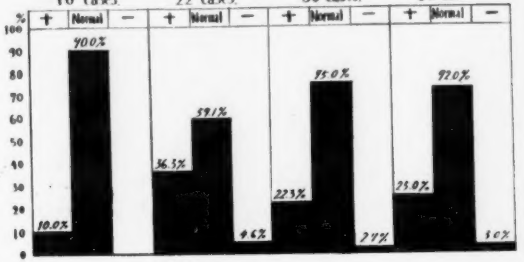


TABLE XVI

Classification Based on Basal-metabolism.

Number of Goiters: 68 cases.

Race	Sex	elevated		normal		reduced		Total	
Japanese Proper.	♂								
	♀	1	10.0%	9	90.0%	0		10	100.0%
	Total	1	10.0%	9	90.0%	0		10	"
Formosans	♂								
	♀	8	36.5%	13	59.1%	1	4.6%	22	"
	Total	8	36.5%	13	59.1%	1	4.6%	22	"
Aborigines	♂	1	25.0%	2	50.0%	1	25.0%	4	"
	♀	7	19.9%	25	78.1%	0		32	"
	Total	8	22.3%	27	75.0%	1	2.7%	36	"
Total	♂	1	25.0%	2	50.0%	1	25.0%	4	"
	♀	16	25.1%	47	73.4%	1	1.5%	64	"
	Total	17	25.0%	49	72.0%	2	3.0%	68	"



also to the goiter type. Grades I and II are diffuse parenchymatous type which are mostly found in the prepuberty period. The nodular goiters are found also in the childhood period, but they also commonly develop after puberty and enlarge in size with the age. Table XIV represents the number and percentage of each grade. Table XV shows the relation between different grades of swelling and the age.

(2) *Classification Based on Function.*—According to the examination performed on 68 cases, the basal metabolism is elevated in 25 per cent of all cases. On the other hand, 3 per cent of all cases are reduced (Table XVI).

TABLE XVII

Classification Based on Functional Effect Produced on the Visceral Nervous System.

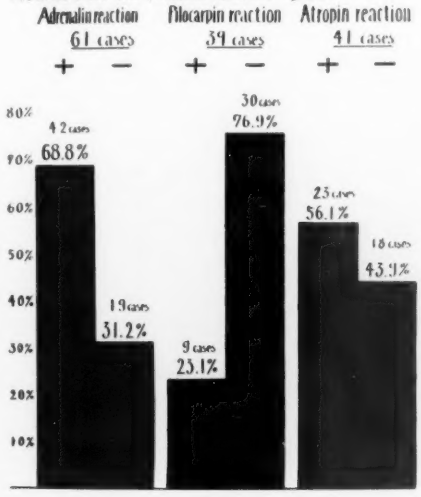
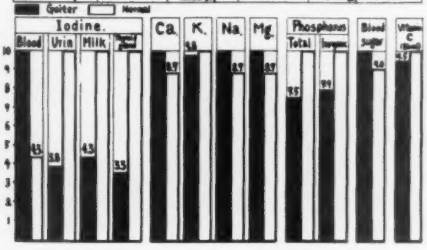


TABLE XVIII

Mineral Metabolism

Bloodsugar and Vitamine.

		Goiters.			Normal.			
		Cases	Max.–Min.	Mean	Cases	Max.–Min.	Mean	
J.	Blood	41	231.65 – 19.035	63.032γ%	32	42.30 – 12.69	27.573γ%	Increased
	Urin	15	1302.89 – 39.105	304.446γ	15	2334.13 – 234.88	804.446γ	decreased
	Milk	5	31.71 – 8.96	16.802γ%	9	48.65 – 12.38	38.772γ%	»
	[illegible]	29	18.50 – 0.199	3.518γ		19.99 – 4.615	10.581γ	»
Ca.		32	15.90 – 10.45	12.09%	19	11.05 – 9.12	10.55%	slightly increased
K.		32	23.04 – 13.30	16.73%	19	19.65 – 16.96	17.06%	almost normal
Ca/K		32	1.53 – 0.70	1.24	19	1.95 – 1.48	1.94	slightly decreased
Na.		4	402.50 – 391.00	401.16%	2	386.30 – 384.10	351.20%	slightly increased
Mg.		4	2.99 – 1.96	2.63%	2	2.38 – 2.25	2.31%	»
P.	Total	36	19.09 – 3.42	8.69%	16	15.67 – 8.99	11.40%	decreased
	Inorganic	36	5.09 – 1.04	3.75%	16	6.63 – 3.35	4.78%	decreased
Bloodsugar		35	126.0 – 89.0	97.5%	6	104.0 – 82.0	88.0%	slightly increased
Vitamin-C		16	2.113 – 0.401	0.882%	14	1.113 – 0.536	0.927%	almost normal



Cretinoid cases, such as are seen in Switzerland, are not frequently encountered. In the highly endemic regions, the Basedow's disease types are not found. However, in 36.3 per cent of the Formosans operated upon, the basal metabolic rates were high. On the other hand, the Japanese proper and the Formosans, in the practically nonendemic regions of Formosa, have the tendency of developing the Basedow type of disease.

According to the function of the vegetative nervous system, relative sympaticopathy is encountered in one-half of the cases (Table XVII).

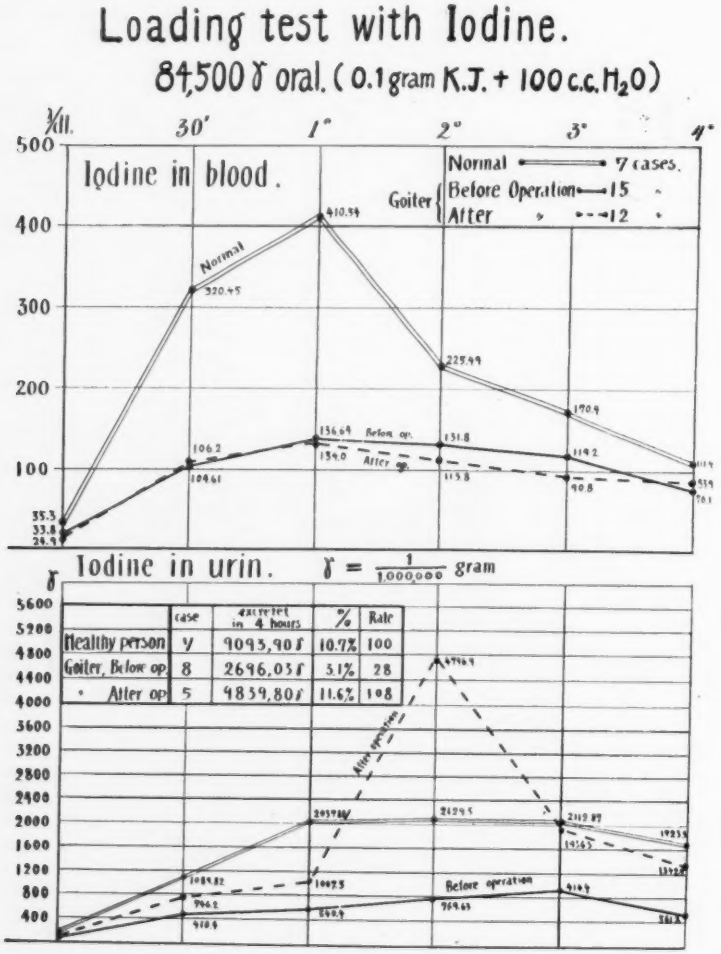
D. Pathologic Physiology.—We have examined the iodine, mineral, sugar and vitamin metabolism of goiter cases.

(1) *Iodine Metabolism* (Table XVIII).—The blood iodine of goiter cases, estimated by Fellenberg's method, increases in many cases about twice that of normal. The mean value in goiter cases is 63.032 micrograms per 100 cc. in comparison to the normal cases of 27.573 micrograms per 100 cc. But

this finding does not agree with that in the other countries. The iodine contents of the blood are high in healthy Formosans.

The excretion of iodine in the urine during 24 hours is less in cases of goiter—309.446 micrograms per day. In the normal the excretion is 809.445 micrograms per day. Likewise, the excretion of iodine in milk is also

TABLE XIX



less than the normal. The content of iodine in extirpated goiter tissues is less than that from healthy glands, notwithstanding its larger volume in weight.

Loading the blood with iodine, by means of giving 0.1 Gm. of KI. with 100 cc. of water, shows that in the goitrous patient the blood iodine increase is less than in healthy persons (Table XIX) before and even after

operations. Likewise the excretion of iodine in the urine for four hours is less, 3.1 per cent, compared with 10.7 per cent in the normal individual. However, it returns to the normal value of 10.7 to 11.6 per cent after resection of the goiter.

(2) *Mineral Metabolism* (Table XVIII).—We have estimated the calcium, potassium, magnesium, sodium, and phosphorus in the blood of goiter cases and healthy persons. The calcium content of the blood increases slightly; the mean value is 12.09 mg./dl., the normal being 10.55 mg./dl.

The magnesium and sodium contents of the blood in the goiter patients also increase a little. The potassium in the blood shows almost a normal value in most cases, thus, the Ca/K index decreases a little. Both inorganic and organic phosphorus in the blood decrease slightly.

(3) *Sugar and Vitamin Metabolism* (Table XVIII).—We have not encountered any hyperglycemia in goiter cases. The blood sugar remained within the normal upper limit. The adrenalin glycemia is depressed in one-half of the cases, although the accelerated and normal cases are about the same. This adrenalin glycemia reaction does not parallel the adrenalin pulse and blood pressure reaction, the basal metabolism, and the execretory function of the liver tested with dye. The double sugar-loading test shows no special findings. There is a disturbance of liver function in one-half of all cases by the azorubin test. On the other hand, the function of the kidney is normal from the standpoint of the dye test. The vitamin C content of the blood is lower than normal.

(4) *Stenosis and Dislocation of the Trachea* (Plate III).—For this study, roentgenograms were taken in 68 cases. Tracheal stenosis were found in 38.1 per cent of them. They occur not only in cases of large nodular goiter but also in instances of the Grade III, diffuse parenchymatous goiter. The stenoses are either circular or saber-form. The dislocation of trachea takes place either from the side or behind, and the distance of the trachea from the vertebrae increased. Dyspnea occurred not infrequently.

(5) *Goiter Heart* (Plate IV).—The hearts of the goiter patients are found to be enlarged in one-half the cases. The right-sided enlargement is much more frequent than the left (26.4 to 17.6 per cent). Bilateral enlargement is found in only 6 per cent of cases. The heart enlargement has no relation to the tracheal stenosis.

SUMMARY

In Japan proper, only sporadic goiters are encountered. Endemic goiters are found only in Formosa. The highest rate in one region in Formosa is 63.5 per cent, in which rate of incidence, 78.8 per cent occur in females, when only the female population is considered.

The Japanese proper in Formosa are less frequently involved; the Formosans come second; and the Aborigines are the most susceptible. The low endemicity among the Japanese proper is accounted for by the fact that seafoods are eaten more generally by them. Nodular goiters are prevalent among

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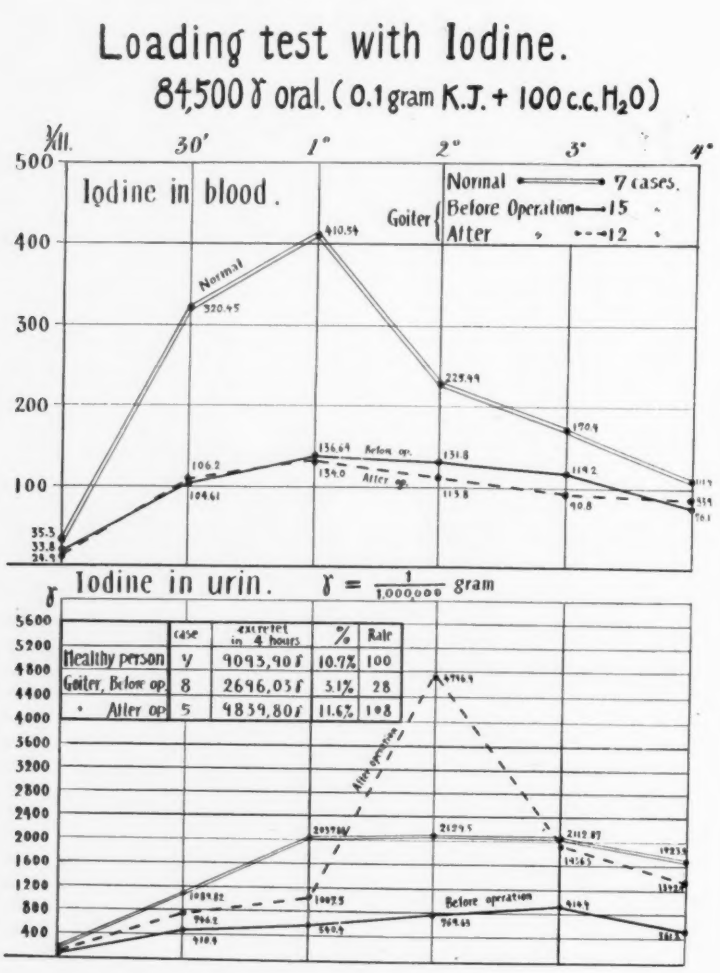
Loading test with Iodine.
84,500 γ oral. (0.1 gram K.J. + 100 c.c. H_2O)
Iodine in blood.
Normal 7 cases.
Goiter Before Operation 15
After 12
Normal
Before op.
After op.
Iodine in urin. γ = 1/1,000,000 gram
Healthy person 7 9093,90 γ 10.7% 100
Goiter, Below op. 8 2696,03 γ 3.1% 28
After op. 5 9839,80 γ 11.6% 108
After operation
Before operation

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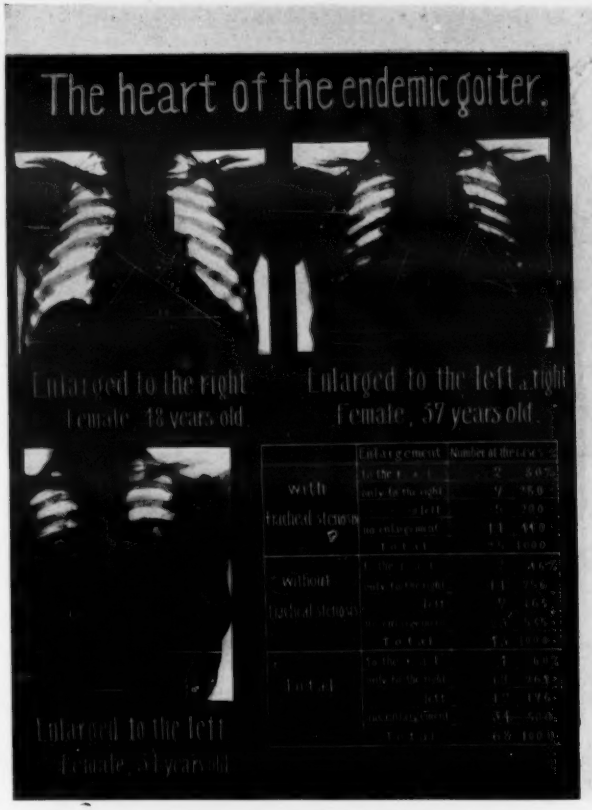
The heart of the endemic goiter.
Enlarged to the right
Female, 18 years old
Enlarged to the left, a right
Female, 57 years old.
Enlarged to the left
Female, 31 years old

PLATE III.—Roentgenograms showing the various types of stenoses encountered, and the degrees of displacement of the trachea.

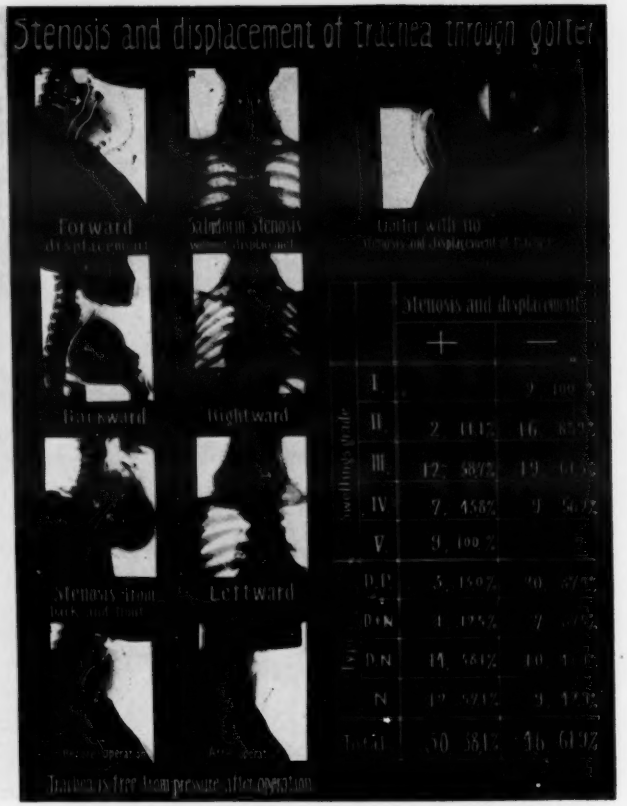

PLATE IV.—Roentgenograms showing the various degrees and direction of enlargement of the heart, and their relevant measurements.

the Aborigines, while the parenchymatous goiters are more common among the Formosans. The basal metabolic rate is increased in about 25 per cent of the cases. The iodine content of the blood is high.

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SURGERY OF THE THYROID IN A LARGE MUNICIPAL HOSPITAL

RODERICK V. GRACE, M.D., AND CARNES WEEKS, M.D.
NEW YORK, N. Y.
FROM THE FIRST SURGICAL DIVISION, BELLEVUE HOSPITAL, NEW YORK, N. Y.

THE PRESENT COMMUNICATION is a study of 360 consecutive cases of thyroid disease treated surgically by members of the Staff of the First Surgical Division, Bellevue Hospital, N. Y. This is one of four surgical divisions in a large municipal hospital of 2,400 beds. The analysis of this consecutive series comprises a ten-year period, from 1930 to 1939, inclusive. Our interest in surgery of the thyroid was stimulated in 1930, when a Thyroid Clinic was established by the authors in our Out-Patient Department. In going over our records it was found that during the preceding ten-year period, 1920 to 1929 inclusive, only 48 patients had been operated upon for disease of the thyroid. During the first year after the establishment of this special clinic, 100 thyroid operations were performed by our staff.

It was said, at that time, that it might be impossible for good surgery of the thyroid to be performed on the general surgical wards of a large municipal hospital. This group of cases has not had the advantages of quiet afforded by small private rooms but have been taken care of in the noisy and busy public wards. They have not had the advantages of special dietary control with measurement of caloric intake. The diet is the Bellevue high caloric diet with extras. Only a very few patients had the services of special nurses.

Due to the great physical distances at Bellevue, it proved impractical to have the close cooperation of the Medical Service, which has been so much stressed by other authors. Our patients, in the great majority of instances, were admitted directly from the Thyroid Clinic to the surgical wards, where their preoperative management was undertaken. The advantages of this plan which was forced upon us, we believe, far outweigh the disadvantages. The patients become accustomed to their surroundings, they get to know the nurses and the doctors, and the latter have the great advantage of seeing the patients daily and are in a better position to evaluate the severity of the disease and the progress the patient is making. Needless to say, medical and other consultations are frequent when the thyroid conditions are associated with such complications as heart failure, pregnancy, diabetes, *etc.*

Naturally, hyperthyroidism is the thyroid condition we are most interested in. Table I shows the distribution of the cases of thyroid disease.

The great majority of our cases were first seen by one or both of the authors in the Thyroid Clinic or on the surgical wards, and their preoperative management was supervised by us. The evaluation of the severity of the hyperthyroidism was made when the patients first appeared in the Thyroid

* Read before the New York Surgical Society, November 22, 1939. Submitted for publication November 3, 1939.

Clinic, and, at this time, it was determined as to whether a one-stage or a two-stage operation was to be performed. We feel that this early decision as to his real condition should be made when the patient is carrying on his normal activities. This is vitally important. An excellent example of how bedrest alone can mask a severe underlying hyperthyroidism is shown by the following case:

TABLE I

DISTRIBUTION OF ALL CASES OF THYROID DISEASE
(1930–1939)

Goiter:		
Toxic Cases:	Exophthalmic goiter	175
	Toxic adenomata	70
		245
Nontoxic Cases:	Adenomata	115
	Total	360

Case Report.—A young girl, age 22, had been referred by another hospital, direct to our wards, as a case of borderline hyperthyroidism. She had been in bed in this hospital for one month, and remained in bed on our wards for another two weeks. She was seen in consultation by a physician with large experience in hyperthyroidism, who made a diagnosis of neurocirculatory asthenia and who advised no operation and discharge to the Psychiatric Clinic. Three days after discharge, the patient returned to our wards to visit a friend and happened to be seen by one of us. She was on the verge of a thyroid crisis, with a pulse rate of 180.

Eleven members of our staff operated upon the cases in this series, independently. To offset the disadvantages of this, a strict regimen was carried out suitable to our service. First, a decision had been reached as to whether or not the patient should be operated upon in two stages. We deplore the custom, adopted on some services, where a decision as to employment of a one- or two-stage procedure is left to the anesthetist at the time of operation. In the Thyroid Clinic, the patient is subjected to the following: Basal metabolic rate; electrocardiogram; exophthalmetric measurements; anterior and lateral roentgenograms of the trachea, for deviation and compression; and examination of the vocal cords. On admission to the surgical wards, the patient is kept at bedrest for a few days and then allowed to be up one hour a day. Lugol's solution, minims 10, t.i.d., and luminal, grains 1, t.i.d., are given. Forced fluids and a high caloric diet are instituted. One basal metabolic determination is made preoperatively, and any gain of weight is determined. More rapid improvement on this regimen than was expected, however, never leads us to reverse our decision from a two-stage to a one-stage procedure. However, if the patient's condition is poorer than we had anticipated, or is complicated by an intervening acute infection, we frequently decide on two stages, rather than the original one-stage.

On analyzing the 175 cases of exophthalmic goiter, we found that most of

the patients were women, that most of them fell in the third and fourth decades, and that approximately 20 per cent were over 45 years of age. The average age was 34.5 years. This is lower than in the cases of toxic adenomata, which averaged 41.8 years. We found a higher proportion of colored people than we expected, 13, or 7.5 per cent. The duration of symptoms among this group was 16.6 months, whereas in the toxic adenoma cases it was 57 months. These patients were hard working people in the lower economic groups and frequently put off seeking medical attention until the last possible moment. We found, however, that the patients suffering from hyperthyroidism in our clinic were considerably above the average type of the very poor Bellevue patient.

TABLE II

ANALYSIS OF CASES OF THYROID DISEASE

	175 Cases Exophthalmic Goiter	70 Cases Toxic Adenoma	115 Cases Nontoxic Adenoma
Sex: Female	138	64	102
Male	37	6	13
Average age	34.5 yrs.	41.8 yrs.	36 yrs.
Colored	13	2	0
Duration of test symptoms	1.3 yrs.	4.8 yrs.	9.7 yrs.
Average loss of weight	25.3 lbs.	20 lbs.	none
Diarrhea	39	1	none
Previous operations	15—8.5%	5—7.1%	1
Previous roentgen ray therapy	3	1	0
Previous iodine therapy	27	9	8

In going over the possible etiologic factors concerned with the onset of hyperthyroidism, we cannot refrain from mentioning the danger of general or interval surgery in patients suffering from hyperthyroidism, before the condition is controlled by thyroidectomy. The authors were able to collect a series of cases in which such procedures as cholecystectomy, removal of rectal polypi, tonsillectomy, extracting teeth, *etc.*, were carried out in persons suffering from hyperthyroidism, with an operative mortality of 30 per cent.

We find that 39, or 22.2 per cent, of the patients suffered from diarrhea. The average loss of weight in 151 cases is 25.3 pounds. Approximately 20 per cent of these lost from 45 to 50 pounds.

We were interested in the fact that 15, or 8.5 per cent, of our exophthalmic group, and five, or 7.1 per cent, of our toxic adenoma group had had previous operations elsewhere, and the majority of them at well known thyroid clinics. We find many of them well for from five to 13 years following their original operation, before recurrence of symptoms. This has impressed us with the importance of long follow-up examinations in this type of patient following operation, and the danger of considering a case cured without adequate follow-up.

Previous roentgenotherapy had been administered in only four of all the

toxic cases, but in one patient it was undoubtedly one of the contributing factors in her postoperative death.

Previous iodine therapy was noted in 14 per cent of our toxic patients. In two cases there was evidence of the patient being "iodine-fast":

Case 1.—The first patient, a young woman physician who had recurrent hyperthyroidism, had been given small doses of iodine for a period of three years. Following operation for removal of rectal polypi, under prolonged anesthesia, the patient went into a severe thyroid crisis and at no time before her thyroidectomy were we able to control her with iodine. She, however, recovered following thyroidectomy.

Case 2.—The second patient was a female, age 35, who had been taking iodine for eight weeks previous to admission. She could not be controlled with iodine, and died in thyroid crisis, following operation.

We find that in this group, 80, or 45.7 per cent, of our patients had exophthalmos at the first examination. This determination is based on actual measurements of the eyes with the exophthalmometer, which gives an accurate idea of the degrees of exophthalmos and does away with the inaccurate impressions gained from the various text-book eye signs. It also gives an accurate evaluation of whether this condition improves or progresses following operation. More will be said concerning this condition in the analysis of our follow-up report. The average measurements were O.D. +20.9; O.S. +20.9.

The average blood pressure readings in the exophthalmic group were: Systolic, 140 Mm. of mercury; diastolic, 73, with a pulse pressure of 67. The readings in the toxic adenoma group were approximately the same.

Systolic murmurs were noted at the apex in 147 out of 245 patients. We do not believe that these murmurs were evidence of organic heart disease but relative mitral insufficiency due to an overacting heart. The great majority of murmurs disappeared after the arrest of the hyperthyroidism by operation.

Auricular fibrillation occurred preoperatively in 15 of the toxic patients, and in only two did it fail to disappear following thyroidectomy.

TABLE III

	175 Cases Exophthalmic Goiter	70 Cases Toxic Adenoma
Exophthalmos	80—45.7%	0
Blood pressure	140/73	147/82
Pulse pressure	67	65
Systolic murmur, apex	107	40
Heart enlarged	101	35
Auricular fibrillation	11	4
Basal metabolic rate:		
Admission	+51.9	+36.5
Ante-operative	+24.0	+20.9
Postoperative	+ 4.4	+ 7.4
Pulse rate:		
Admission	118	109
Ante-operative	84	84
Postoperative	84	84

The average basal metabolic readings in the exophthalmic group were: On admission, plus 51.9 per cent; before operation, plus 24 per cent; and postoperatively, plus 4.4 per cent. The basal metabolic figures in this group, before treatment was instituted, were somewhat higher than similar figures of the toxic adenoma group, which were plus 36.5 per cent (Table III).

The most severe complication we encountered was that of severe tonsillitis in very toxic cases. The majority of our patients have both diseased tonsils and bad teeth. Before the introduction of sulfanilamide, their treatment necessitated prolonged bedrests. It was also responsible for the decision that a two-stage procedure would be safer. This complication was the immediate cause of preoperative crises and one of our postoperative deaths. Eight patients having rheumatic heart disease were successfully operated upon (Table IV).

TABLE IV

	175 Cases Exophthalmic Goiter	70 Cases Toxic Adenoma
Complications:		
Severe tonsillitis	10	0
Rheumatic heart disease	7	1
Hypertensive heart disease	2	2
Diabetes	4	2
Pregnancy	3	0
Rheumatic fever	1	1
Pulmonary tuberculosis	1	1
Operations:		
Partial thyroidectomy: One-stage	127	70
Two-stage	47	1
Ligation superior thyroid arteries	1	0

The average pulse rate on admission was 112; just before operation it was 84; and on discharge 84.

All of our toxic patients, except two, had preoperative iodine administered. These patients were mistakenly thought to have nontoxic adenomata, and Lugol's solution was not given. Both were actually toxic and had severe postoperative reactions.

Eleven surgeons performed 293 operations on 245 patients suffering from hyperthyroidism, with four deaths, a mortality of 1.6 per cent (Table V). On September 16, 1932, on the occasion of our last death, two-stage operations were instituted, and since that time, seven years ago, we have operated upon 27.4 per cent of all our cases in stage-procedures, with no deaths. No patient suffering from hyperthyroidism has been refused operation.

Avertin and gas-oxygen anesthesia was used in 246 cases. Since the establishment of the Anesthesia Department at Bellevue, avertin and cyclopropane have been used 49 times. Local anesthesia has been employed in only nine instances. We have found avertin, as a basal anesthetic, to be highly successful, the patient arriving in the operating room oblivious of his surroundings.

Severe postoperative reactions occurred in 18 instances, or 6.1 per cent. These patients were treated by continuous infusion of glucose, ice packs, iodine, sedatives and the use of the oxygen tent.

TABLE V

MORTALITY STATISTICS

	Number	Deaths	Per Cent
Toxic Cases	245	4	1.6%
Exophthalmic goiter	175	3	1.7%
Toxic adenoma	70	1	1.4%
Nontoxic adenoma	115	0	0

Appended is an analysis of four deaths, all occurring during the first three years of this series:

ANALYSIS OF POSTOPERATIVE DEATHS

Case 1.—B. W., white, male, age 43, Jewish, was admitted to the hospital, July 16, 1931, and died July 29, 1931. His chief complaints were nervousness, palpitation, loss of 30 pounds of weight in five months. A diagnosis of exophthalmic goiter was made. His B.M.R. was plus 55. He was put on iodine medication for 13 days; a subtotal thyroidectomy was performed under avertin and gas-oxygen anesthesia. His pulse never went over 110 during the operation, and his condition was considered excellent. However, the patient died 12 hours later in a thyroid crisis. This is the moderately severe type of thyroid case that we now operate upon in two stages.

It was poor surgical judgment to have operated upon this man in one stage. We might bring up, in connection with this case, the danger of leaving to the anesthetist the decision as to whether both lobes should be removed at one operation. After removing this patient's right lobe and isthmus, his condition was excellent, yet it is obvious that we should have terminated the operation at that time.

Case 2.—C. J., female, age 30, Colored, was admitted to the hospital, March 9, 1932, and died April 17, 1932. Her chief complaints were nervousness, palpitation, sweating, and loss of 50 pounds of weight in one year. She was an extremely sick exophthalmic goiter case, with a B.M.R. of plus 58. Her exophthalmos measured O.D. plus 21; O.S. plus 21. On the twelfth day following admission, she developed a severe hemolytic streptococcus tonsillitis. Unfortunately, iodine medication was then withdrawn for nine days. On her twenty-fifth day, she went into a thyroid crisis with delirium. She improved with the usual treatment but, on the thirty-sixth day, she was thought to be losing ground, there was no response to iodine so that both superior thyroid arteries were ligated under local anesthetic. This was undertaken in her own bed. She died 24 hours later, in a thyroid crisis.

Obviously iodine should not have been withdrawn just when she needed it most. It was a desperate cause, but we still think that ligation of the arteries was justified.

Case 3.—A. C., female, age 35, was admitted to the hospital, August 31, 1932, and died September 16, 1932. Her chief complaints were nervousness, palpitation, and loss of 50 pounds of weight in two years. She was an extremely ill case of exophthalmic

goiter, with a B.M.R. of plus 94. She had been taking iodine for eight weeks but had discontinued it one month before admission. It was impossible to control this patient with iodine; her weight dropped from 96 to 79 pounds. In spite of this she was operated upon, 16 days after admission. Following removal of the right lobe the patient went into extremis and died after several hours.

Death in this case was due to poor surgical judgment. She was obviously iodine-fast, and should have had prolonged bedrest followed by preliminary lobe ligations.

Case 4.—M. C., female, age 51, was admitted to the hospital, May 4, 1932, and died May 16, 1932. Her chief complaints were goiter, cough, and dysphagia, for 18 years; large veins on the neck and chest for four years, and nervousness for three years. She had been treated in the Medical Department for three years, during which time she had roentgen ray treatments. Her B.M.R. was plus 37. The diagnosis was hyperthyroidism, associated with an enormous intrathoracic adenoma, causing obstruction of the trachea, and the superior vena cava. She weighed 85 pounds. Following ten days of iodine therapy, an extremely large intrathoracic goiter was removed under avertin, and local anesthesia. She did well for 24 hours, and then died in a delayed thyroid crisis.

We believe that if operation could have been performed three years earlier, and before roentgenotherapy was instituted, the patient might have had a better chance of survival.

Mild infections occurred in 25 instances, and included wounds showing but one drop of pus—the offending organism was usually *Staphylococcus aureus*. Severe infection occurred four times—the organisms recovered were hemolytic streptococcus twice and colon bacillus twice. Catgut was used in all operations but two. All but two wounds were drained. The incidence, then, of postoperative wound infection in 408 operations was 7 per cent.

Postoperative hemorrhage occurred seven times, or 1.7 per cent. All patients were reoperated upon on the same day, and the bleeding controlled. All these patients recovered. One case required tracheotomy and developed bilateral, massive atelectases.

Small hematomata developed in 22 wounds and were evacuated. Three large hematomata, from slow oozing, developed and caused tracheal obstruction. These were evacuated, causing relief of the obstructive symptoms.

The trachea was inadvertently opened in three of 413 operations. All were repaired immediately. No wound infections resulted in any case. One trachea fistula closed spontaneously one month later. It had never communicated externally.

Injury to one of the laryngeal nerves occurred seven times, or 1.7 per cent. One patient was hoarse for one year, one for six months, and three cleared up before leaving the hospital. One patient is still hoarse, after three years; the others all have normal speaking voices. In two cases, one nerve had been injured during a previous operation elsewhere, and following further operation, developed temporary bilateral cord paralyses. Both cases had intratracheal catheters introduced, one for 24 hours, and the other for 48 hours. Fortunately, the recent injury proved only of a temporary nature (Table VI).

TABLE VI

POSTOPERATIVE COMPLICATIONS

	Exophthalmic Goiter	Toxic Adenoma	Nontoxic Adenoma	Totals	Per Cent	
Number of operations	222	71	115	408		
Severe reactions	16	2		18	6.1%	
Infections: Mild	18	3	4	25	6.+%	7.0%+
Severe	4	0	0	4	1.0%	
Postoperative hemorrhage	4	0	3	7	1.7%	
Hematoma: Large	2	0	1	3	0.7%	6.0%+
Small	9	6	7	22	5.6%	
Tracheal injury	3	0	0	3	0.7%	
Recurrent laryngeal nerve injury	5	1	1	7	1.7%	
Tetany: Mild	3	0	0	3	0.7%	0.9%
Severe	1	0	0	1	0.2%	
Myxedema: Mild	7	0	0	0	2.9%	

Of 360 patients operated upon for thyroid disease, 345, or 94 per cent, have been followed for from six months to ten years. All of these cases have been actually examined by one of the 11 operators, and most of them have been seen by one or both authors, in the Thyroid Clinic.

TABLE VII

FOLLOW-UP RESULTS—345 OUT OF 360 CASES—94 PER CENT

	Exophthalmic Goiter	Toxic Adenoma	Nontoxic Adenoma
Number of cases	170	66	109
Average gain in weight	22	16.6	
Average pulse pressure	85	81.7	
Average blood pressure	130/80	142/98	
Pulse pressure	50	56	
Average basal met. rate	+7	−2	
Recurrence	14—8%	1—1.4%	6—5.2%
Excellent	164—96.4%	64—96.9%	104—95.4%

The average gain in weight among the toxic group was 22 pounds. The average blood pressure in the exophthalmic group has been reduced from 140/73 to 130/80, with an accompanying fall in the pulse pressure from 67 to 50. The figures for the toxic adenoma group are not striking, probably due to the older age-group—147/82 as compared to 148/92, the pulse pressure falling from 65 to 56.

The average basal metabolic rate, for all toxic cases followed, is plus 3 per cent (Table VII).

The average exophthalmetric readings on those having exophthalmos before operation was O.D. plus 20.9; O.S. plus 20.9; these same patients in follow-up showed measurements of O.D. plus 21; O.S. plus 21. The current feeling has been, we believe, that, of those patients suffering from exoph-

thalmos associated with hyperthyroidism, at least 50 per cent get well. Our figures do not bear this out, and we feel very strongly that if accurate measurements of the eyes are taken with the exophthalmometer it will be discovered that the exophthalmos does not improve.

We have had one case of progressive exophthalmos in a female, age 21. She had a partial thyroidectomy performed for severe hyperthyroidism, and six months later was reoperated upon for persistence of symptoms. Following this, there were no hyperthyroid symptoms, but ten months later her exophthalmos increased from O.D. 25; O.S. 24, to O.D. plus 30 (well over the highest measurement on the instrument); O.S. 27. She developed marked edema of her conjunctivae but no corneal ulceration. On June 1, 1938, Dr. Joseph King performed a one-stage Naffziger operation on the right side, and on December 12, 1938, a similar operation on the left side. Her present readings are O.D. 25; O.S. 24, which are the same as before the progressive exophthalmos started.

A tarsorraphy was performed by Dr. Webb Weeks, in one case of unsightly but not progressive exophthalmos, which resulted in an excellent cosmetic result.

Recurrence or persistence of hyperthyroid symptoms following operation has occurred 15 times in 236 followed cases, or 4.2 per cent. This includes two patients in whom it recurred twice. It recurred in only one patient operated upon for toxic adenoma. Four patients, following operation, showed persistence of hyperthyroid symptoms within a very few months. We do not believe that these cases had a radical enough primary operation. Of all the recurrent and persistent cases, ten have been reoperated upon and are well, three refused reoperation, and one mild recurrence is doing well with occasional small doses of iodine (Table VII).

There have been seven occurrences of mild postoperative myxedema, an incidence of 2.9 per cent. All have been controlled by thyroid extract feedings and at their last follow-up visit were free of symptoms.

Postoperative tetany has occurred three times in a mild form and was controlled by calcium feedings. One severe case followed operation for a second recurrence. This patient had moderate to severe symptoms for six years, well controlled by calcium. At the present time there is no evidence of tetany and calcium feedings are not required.

We have one interesting case of pituitary dyscrasia in a young girl who, during 11 months previous to her operation, gained 54 pounds. She was given injections of antuitrin S., in the Endocrine Clinic, and very soon developed typical symptoms of hyperthyroidism. Following partial thyroidectomy she lost 50 pounds, and at present is normal.

Of the 236 toxic cases followed, 228, or 97.3 per cent, are classed as excellent results.

One hundred nine cases out of 115 cases of nontoxic adenoma were followed. Recurrence occurred in six cases, or 5.2 per cent. One recurrent case became toxic, with a basal metabolic rate of plus 41 and loss of 16 pounds

in weight. Five patients refused reoperation, including the toxic one. One has been reoperated upon and remained free of recurrence for four years. One hundred four out of 109 patients followed in this group are considered excellent results, or 95.4 per cent.

CONCLUSIONS

(1) That the preoperative use of iodine is a purely surgical procedure.

(2) That the postoperative regression in exophthalmos is apparent, and not real.

(3) Surgery of the thyroid can be undertaken in a large municipal hospital by a group of surgeons with a reasonably low mortality rate.

DISCUSSION.—DR. A. S. MCQUILLAN (New York) offered the suggestion that in some desperate cases the inferior thyroid vessels be ligated as well as the superior. They are larger in caliber. Doctor McQuillan has many times ligated these vessels along with the superiors and the patient has often derived more benefit from ligation of the inferior vessels than from the superiors—preparatory to performing a resection later. It can be very easily accomplished through a transverse incision on a level at which one plans to make the incision for resection later on. The operation is much like the one for avulsion of the phrenic nerve. The inferior thyroid vessels lie just internal and a little anterior to the anterior scalene muscle. This point of ligation is a considerable distance away from the inferior laryngeal nerve. It is probably due to the size of the vessel and shutting off the greater blood supply to the gland that the best results occur.

When should stage-operations be performed? What influences the surgeon's judgment? Too much reliance cannot be placed on the basal metabolic rate. One low rate is better than many high rates. If the metabolic rate is over 30 there is danger, that is, in conjunction with other criteria. More than a favorable metabolic rate is gain in weight, especially recent—evidence that the patient is a fair risk. Persistence of such symptoms as tremor, excessive perspiration, and frequent bowel movements show severe toxicity. A pulse rate of more than 100 is not desirable. Mental symptoms indicate severe toxicity.

Occasionally, a patient may appear to be a good risk, until under an anesthetic, when signs such as a rising pulse rate or a rising blood pressure will appear. Then one must be ready to change his plan. At Bellevue Hospital the blood pressure is taken on every patient operated upon, and a rising blood pressure and pulse rate means a great deal. If that goes up during the first half of the procedure, one should make his plans to take out only one lobe. Also, if the patient takes a poor anesthetic, this is a sign that the patient will not do well.

Doctor McQuillan agreed that surgery, other than thyroid surgery, should not be undertaken on toxic thyroid patients unless in case of emergency.

With regard to the treatment of thyroid crisis, intravenous fluids with glucose, the oxygen tent and sedatives are commonly employed and are most valuable. The postoperative use of iodine is of doubtful value, according to most authorities. Personally, Doctor McQuillan felt unable to state that it is useful. There is some reason for giving thyroid gland substance in these crises. The latter may be due to a deficient thyroid hormone rather than too much of a normal one. It is difficult to understand how the small amount of thyroid tissue left after a subtotal thyroidectomy can function only after a

period of time has elapsed. This tissue has suffered too much trauma to function soon after operation, and it is soon after operation that thyroid crisis appears. Parallel with this reasoning, Rienhoff, at the last meeting of the International Goiter Congress, reported involution of hyperplastic thyroid tissue and amelioration of symptoms as a result of feeding thyroid substance. Also improvement of malignant postoperative exophthalmos has been noted following feeding of thyroid substance. Doctor McQuillan frequently gives thyroid extract to patients with crises—resulting in a lowered heart rate—thus relieving the strain until this self-limited storm has passed. There is a fraction of the thyroid hormone which stimulates the autonomic or vagus system, thus slowing the heart. This was first used in Bellevue, some 20 years ago, by the late Dr. John Rogers.

With regard to the three cases described by Doctors Grace and Weeks, Doctor McQuillan commented as follows: The first patient had been desaturated for six weeks. Then she was given iodine for two weeks prior to operation. The point is that she had had iodine off and on for a year, and had had her hyperthyroidism for a year, and it is only recently that Doctor Lahey made a statement that if an individual has been toxic—has been ill for a year at least with hyperthyroidism—he considers that one of his criteria for performing a stage-operation. This case, however, had only a moderate rise in basal metabolic rate and symptoms of a mild type, no loss of weight, even though there was no gain. She might have done better in a stage-operation but she seemed a good risk on the basis of the usual criteria. The second patient should have done well. She had had iodine over the proper time and seemed in good shape. This is one of the cases that seemed a good risk, but which occasionally develop a crisis. They are not common. Doctor Lahey calls them apathetic cases—not showing their symptoms well. Usually, the patient is an older individual whose response to stimuli is less, due to aged tissue, perhaps, and whose symptoms are not as pronounced as in the younger patient. The third case was a well recognized toxic and hazardous one all the way through, and in this patient the stage-procedure was the only safe way.

Dr. William Barclay Parsons (New York) said that even at the risk of repeating a point, he wished to state his firm support of Doctors Weeks and Grace in their idea of making an early decision on staging or not staging. But if one decides previously to perform a one-stage operation, he must always be ready to move in the direction of two stages at the time of operation if the findings indicate it, but should not change a decision to do a two-stage operation in favor of a one-stage procedure.

Dr. Charles Gordon Heyd (New York) said that it is readily apparent that there is a dilemma in thyroid surgery. Some surgeons give iodine to prevent thyroid crises. Others give iodine to bring about a resolution of thyroid activity, and a small group give thyroid substance after operation to avoid, if possible, thyroid crises. Doctor Heyd places very little confidence in basal metabolic rates as indicating when to operate, or as predicating any degree of recovery in hyperthyroidism. A young girl, of 21 years, with an exophthalmic goiter and a basal metabolic rate of 50, 60 or even 70, will withstand a subtotal thyroid resection with greater ease and safety than a woman of 55 years, with a basal metabolic rate of 20. Iodine has been used much too often and in too great a quantity. At the New York Post-Graduate Hospital sodium iodid, Gr. vii, once a day, intravenously, has been used for three to four days prior to operation, and has served to shorten the period of

preoperative preparation. The most outstanding aid in adequate preparation for operation is bed rest, complete and absolute.

Mortality in a measure is a matter of "the run of cases." There is much too great emphasis placed upon mortality. In any of the modern goiter clinics the mortality rate is a splendid achievement of surgery and the low mortality in the paper of Doctors Weeks and Grace indicates the excellent results of thyroid surgery.

Malignancy in goiter surgery is always to be considered. It occurred 15 times in 627 cases in the Post-Graduate Hospital clinic, with a mortality of 3 per cent. There are certain types of goiter that should be without any mortality. In nontoxic goiter at the New York Post-Graduate Hospital, from 1923 to date, there were 237 operations with no mortality. In the same period there were 103 toxic adenomata with 2.9 per cent mortality. In regard to the hyperthyroidism of Graves' disease type, from 1934 to 1939, there were 108 thyroid operations with no mortality, and there has been no mortality in the last 135 consecutive operations for Graves' disease, while for the period from July, 1935, to date there were 237 patients operated upon for Graves' disease with a mortality of 4.2 per cent.

In toxic, nodular goiters the surgeon is dealing with patients in the fourth, fifth or even the sixth decade of life, whereas in the goiters of Graves' disease type the patients are young with an acute toxemia.

The paper by Doctors Weeks and Grace indicates that surgery of goiter has passed out of the realm of goiter surgeons. With coordinated preoperative treatment and standardized operative technic, the 11 surgeons who contributed to this series have indicated the great degree of safety that appertains to goiter surgery and the limited mortality that may be obtained by any well-trained surgeon.

Dr. Richard Lewisohn (New York) disagreed with the statement that thyroid surgery should be the domain of the general surgeon. In order to obtain good results and to keep the mortality at a low level, surgery of the thyroid should be kept in the hands of those who are specially trained for this work. Otherwise results would not be as good as those reported here tonight by Doctors Grace and Weeks.

BRANCHIAL CYSTS AND SINUSES

FRANK H. LAHEY, M.D.,

DEPARTMENT OF SURGERY,

AND

HARLAN F. NELSON, M.D.,

FELLOW IN SURGERY,

THE LAHEY CLINIC,

BOSTON, MASS.

BRANCHIAL CYSTS AND SINUSES have been of interest ever since they were first reported by Hunczowski in 1789. Their etiology has never been satisfactorily explained although at present Wenglowski's[8] theories as to their origin are most usually accepted. No one type of treatment has found universal acceptance, and, although a large number of clinical discussions on this subject are reported, end-result studies are infrequent.

The treatment of any tumor or sinus of the neck requires an understanding of the many different pathologic entities which may arise in this region. The early recognition of branchial cysts and sinuses is important if they are to be properly managed.

In view of these facts, it seems of value to report 27 cases of branchial cysts and sinuses in which operation was performed at the Lahey Clinic during the past ten years, to comment on the embryology, differential diagnosis, the various plans of treatment that have been outlined in the literature, and end-result studies in our series of cases.

Wenglowski's work is based on anatomic and embryologic studies of a series of 246 cadavers and 75 embryos. His theory as to the etiology of branchial cysts and sinuses has been interpreted by Meyer.[6] This interpretation is generally recognized.

Meyer stated that the beginning of the branchial apparatus takes place in the second half of the first month of embryonic life, and in the course of the second month it completely disappears. The branchial apparatus extends forward, upward and orally. The pharyngeal apparatus extends posteriorly downward and below the mouth. The arches tend to grow closer in embryonic life, until the cleft disappears and the epithelium is displaced outward by the mesenchymal growth or by adhesion and obliteration.

The first arch forms the lateral portion of the upper lip and maxilla, the lower lip and mandible, and the body of the tongue. The second arch makes up the body of the hyoid bone, the stylohyoid ligament and muscle, the anterior portion of the base of the tongue, and the arcus palatoglossus. The third arch forms the greater cornu of the hyoid bone, the posterior portion of the base of the tongue, and the arcus pharyngopalatinus. The

Submitted for publication June 28, 1940.

fourth, fifth and sixth arches go to make up the soft parts of the neck surrounding the greater cornu of the hyoid.

The first cleft forms the external auditory canal and the lobe of the ear; the second cleft, the tonsillar fossa; the third cleft, the thymus; and the fourth cleft, the lateral lobes of the thyroid gland.

Meyer believes that the branchial apparatus belongs to the head and not the neck, and that any congenital pathologic condition referable to the branchial apparatus in human beings must rest along the mandible adjacent to the hyoid bone and the cornu of the hyoid bone. Nothing, in his opinion, below the lower level of the hyoid bone has any genetic relation to the branchial apparatus and all congenital anomalies caused by incomplete retrogression of the branchial apparatus must be located in the region around or above the lower border of the hyoid bone. Any congenital anomaly below this level is in definite relationship with the pharyngothymic duct and must be classified as a lateral cyst or fistula originating from this duct.

Bailey[1] believes that he disproves Wenglowski's theory that the branchial apparatus never leaves remnants in the neck below the level of the hyoid bone by citing a case of a persistent branchial cartilage found in the lower third of a child's neck, a position where a branchial fistula commonly opens.

Many other theories as to the origin of this condition are presented in the literature, and it must be assumed that the etiology of branchial cysts and sinuses is as yet not settled.

This condition is usually found in the younger age-groups and predominates in females. In our series, 56 per cent of the cases occurred in patients under 30 years of age. Seventy per cent of our patients were females.

Branchial fistulae are generally classified into three types: (1) Complete fistula, having both an internal and an external opening; (2) incomplete fistula, having either an internal opening alone and classified as an incomplete internal fistula; or (3) an external opening alone and being classified as an incomplete external fistula.

The usual symptoms that are attributed to branchial cysts and sinuses are a tumor of the neck; a sinus with an intermittent or continuous discharge of secretion; and recurrent attacks of inflammation. Occasionally, an unexplained cough may be attributed to a tract which has become adherent to the vagus nerve. In our series a swelling in the neck, a discharging sinus, and recurring attacks of inflammation were the presenting chief complaints. The duration of symptoms in our group extended from three days to 20 years, the average being four and one-half years.

The diagnosis of branchial cysts and sinuses is frequently difficult, and in our group only 57 per cent were diagnosed correctly previous to operation. Many conditions which commonly occur in the neck must be considered. Among these are: (1) Dermoid cysts. Tumors of this type can usually be differentiated by their content; hair and other foreign elements are frequently found. (2) Cystic hygromata. These tumors are usually

transparent and can be transilluminated. (3) Lipomata. Aspiration of these tumors reveals no fluid content, and their lobulated characteristics to palpation and firmness are suggestive. (4) Thyroglossal cysts and sinuses invariably occur in the midline, are attached to the hyoid and shift position with swallowing. (5) Tuberculous adenitis and sinuses in the neck may be very difficult to differentiate but their matted consistency and other foci of tuberculosis are suggestive. (6) Venous hemangiomata are usually deep-seated. Palpation of these tumors suggests the condition. (7) Deep cervical abscesses are characterized by local tenderness, induration, and systemic reactions. (8) Actinomycosis is rare but examination of the discharge will demonstrate the ray fungus. (9) Hodgkin's disease. An accurate differential diagnosis of this condition may require a biopsy. (10) Lymphosarcoma can usually be differentiated by the fact that it consists of a group of fused

FIGS. 1 and 2.—Typical example of branchiogenic cysts. Note the usual position anterior to the sternomastoid muscle and below the angle of the jaw.

adherent nodes. (11) Lymphatic leukemia can be diagnosed by blood studies and the usual physical findings of leukemia. (12) Carotid body tumors are found at the bifurcation of the carotid vessels and are characterized by a firm, elastic consistency. These tumors may or may not transmit an arterial pulsation. (13) Various cervical metastatic neoplasms may require biopsy for the establishment of the diagnosis but the finding of a primary growth is always suggestive.

Branchial sinuses and cysts in our experience have occurred in about equal frequency on both sides of the neck. Fifty-six per cent were found on the right and 40 per cent on the left. In one of our cases (4 per cent) the fistulae were bilateral.

A diagnosis of branchial cyst or sinuses can, therefore, be established ordinarily by remembering that they will be found in the neck anterior to the sternomastoid muscles, from the angle of the jaw to just above the clavicles, are of a congenital nature, and do not have any of the specific conditions mentioned above (Figs. 1 and 2).

Various types of treatment of this condition have been reported. Cutler and Zollinger[4] have advocated the employment of a sclerosing solution in the treatment of small branchial fistulae. Beck,[3] also, has advocated this treatment in fistulae of this type in infants. The danger of perforation

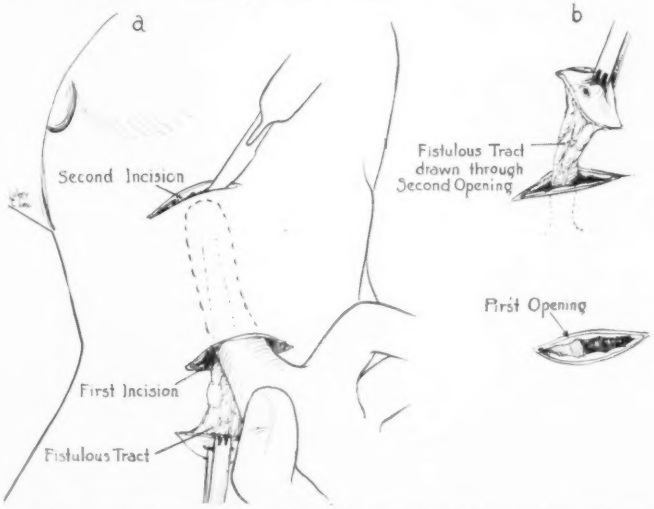

FIG. 3.—The stepladder method of surgical excision of branchiogenic cysts and sinuses. A transverse elliptical incision is first made around the external opening, the sinus tract dissected upward along the sternomastoid muscles. Care must be taken of the great vessels. A second transverse incision is then made at a higher level in the neck parallel with the first, and the dissected branchial fisula is then brought out through this second incision.

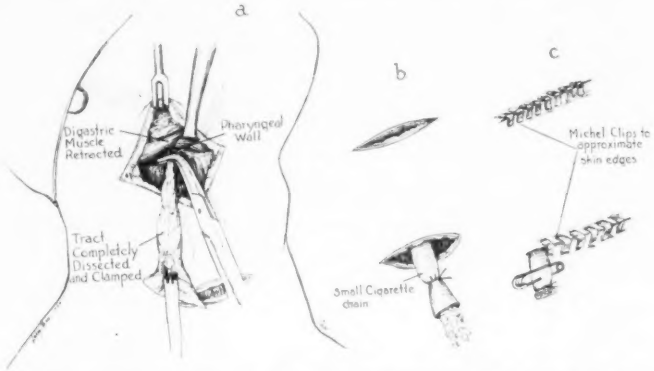

FIG. 4.—The dissection is then carried posteriorly to the wall of the pharynx where the tract is sectioned. We do not believe that inversion of the fistulous tract into the pharynx is necessary. The hypoglossal nerve is commonly seen in this part of the dissection and must be avoided. The wounds are closed about a small rubber-dam drain.

of the pharynx by necrosis and the marked inflammatory reaction which may result are objections to this type of treatment.

A majority of surgeons advocate complete excision of the sinus tract or cyst and suggest various methods. Beck has advocated the use of a collar incision for this procedure, such as is employed in operations on the thyroid. von Hoeker[7] suggests the insertion of a probe into the tract with fixation of the tract to the probe by a ligature, which he believes facilitates

removal. Baumgartner[2] emphasizes the importance of inverting the stump of the fistula into the cavity of the pharynx whenever possible. Gaston,[5] reporting a series of 29 cases from the Cleveland Clinic, does not believe that the inversion of the stump of the fistula into the cavity of the pharynx is necessary, although he agrees that complete surgical extirpation of the tract is essential.

Bailey[1] uses the so-called stepladder method of surgical excision, and this operation has been utilized in the majority of our cases (Figs. 3 and 4). A transverse incision is first made about the external orifice. The skin is freed-up, gentle traction is then exerted on the fistulous tract, and the dissection carried up around the tract as far as possible. At this point, a second transverse incision is made parallel with the first, at a higher level, and the tract is brought up from the first incision out through the second higher incision. This allows an adequate exposure during the dissection of the tract up to the wall of the pharynx, where adequate exposure is so essential.

At times, it may be of assistance to place one finger inside of the mouth and apply pressure against the pharyngeal wall so that danger of perforation of the pharyngeal wall can be minimized. We do not think that inversion of the fistula into the pharynx is necessary and have never done it.

Treatment may have to be modified because of previous unsuccessful attempts at removal. In 34 per cent of our cases previous operation or roentgenotherapy had been carried out.

At the Lahey Clinic, follow-up studies have been made in 27 cases, occurring during the last ten years. In all cases complete surgical excision, as described previously, was performed. Recurrence has not taken place in any of the cases.

SUMMARY

The embryology of branchial cysts and sinuses has been reviewed. The differential diagnosis has been presented, and various plans of treatment outlined.

End-results are reported in 27 cases in which complete surgical excision was performed.

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INTRA-ABDOMINAL APOPLEXY

J. Edward Berk, M.D., M.Sc. (Med.), N. S. Rothschild, M.D.,

AND

J. C. Doane, M.D., F.A.C.P.

Philadelphia, Pa.

FROM THE MEDICAL AND SURGICAL SERVICES OF THE JEWISH HOSPITAL, PHILADELPHIA, PA.

Spontaneous hemoperitoneum is not too unusual an occurrence. Even excluding spontaneous hemoperitoneum, of genital origin in the female, Morridor and Olivier[1] were able to collect 432 cases from the literature. On the other hand, massive spontaneous intraperitoneal hemorrhage resultant from the rupture of a small intra-abdominal blood vessel independent of any direct trauma to the abdomen, is a rare accident. The condition has very aptly been designated "intra-abdominal apoplexy," to denote its close resemblance both in spontaneity and nature to the much more frequent and better known cerebral apoplexy. An exhaustive study of the literature has revealed but 19 cases which might be so classified.* To these 19, we have added a case of our own and briefly tabulated (Table I) what seemed to us the essentials in each. It is only through the repeated reportings and tabulations of such cases, that characteristics, if any, will become recognized which may serve in the diagnosis and treatment of future cases.

Case Report.—The patient, male, age 52, presented himself at the hospital at 10:00 P.M., May 2, 1939, complaining of dull, persistent pain in the abdomen since April 29, 1939, which had become steadily worse. The pain, which began insidiously, was constant, dull, and diffuse over the midabdomen without any radiation. Vomiting had occurred but once, and that was on the day of admission. The vomitus was of a nondescript type. The bowels had been regular and the appetite undisturbed. There were no urinary symptoms.

The patient had known for several years that he had hypertension. For the past two months he had been receiving treatment for attacks of precordial pain and dyspnea which would occur while walking home from work. He had had a bilateral herniorrhaphy and appendicectomy in 1935. For the past few years he had noted failing vision. There was no history of any digestive disturbances. The remaining past history and the family and social history were irrelevant.

Physical Examination.—As seen on admission, the patient was resting flat in bed apparently fairly comfortable, despite his description of pain of a rather severe character. The state of nutrition was fair. There was no cyanosis, jaundice or dyspnea. He appeared alert, oriented and cooperative. Temperature 98° F.; pulse 90; respirations 21; blood pressure 240/170.

The heart was markedly enlarged. There was a presystolic gallop rhythm present with a systolic murmur at the apex and base and a split pulmonic second sound. The aortic second sound had a tambour quality. The abdomen was flat and the wall was soft and relaxed. Tenderness was obtained in the epigastric area on deep pressure. The

Submitted for publication January 8, 1940.

* Since this paper was submitted an additional case has been reported (Crile, G., Jr., and Newell, E. T., Jr.: Abdominal Apoplexy, J.A.M.A., 114:1155, 1940).

peripheral blood vessels were firm and thickened. Ophthalmoscopic examination revealed a blurring of the disk margins and hypertensive neuroretinopathy, Grade III. Because of the marked hypertension, the apparent cardiac and arterial changes and the essentially negative abdominal findings, a tentative diagnosis of "abdominal angina" was made and the patient was kept at rest in bed under observation.

Laboratory Data.—W.B.C. count on the morning following admission was 16,000, 86 per cent neutrophiles. Repeated counts yielded figures ranging between 10,000 and 14,200 W.B.C.

An electrocardiogram revealed myocardial disease with an intraventricular conduction defect. A flat roentgenogram of the abdomen was negative and a gastro-intestinal roentgenologic examination revealed nothing more than spasticity in the pyloroduodenal region. Repeated uranalyses showed a low specific gravity with a profusion of casts and W.B.C. Repeated kidney function tests, likewise, showed impaired renal function. The blood Wassermann was negative. All other studies yielded results within normal limits.

Course in Hospital.—The presenting complaint of diffuse midabdominal pain of a dull nonradiating type persisted after admission until May 8, 1939. On the evening of May 8, 1939, the temperature began to mount to reach a high of 103° F. at noon of May 9, 1939, then declined to return and remain normal about noon of May 10, 1939. The patient was completely asymptomatic and examination revealed nothing to account for this temperature elevation other than slight distention of the abdomen. A repeat roentgenogram of the chest and electrocardiogram were both negative. Abdominal distention remained, despite regular bowel evacuations and a lack of any complaints on the part of the patient.

Shortly before 3:00 A.M., May 16, 1939, the patient complained of sudden severe, nonlocalized abdominal pain and requested a bedpan. While on the bedpan he vomited about ten ounces of a dark material that seemed blood-tinged, following which he went into a partial collapse. Examination revealed a temperature of 98° F. (rectal), pulse 98; respirations 28; blood pressure 90/70. The skin was cold and clammy. The abdomen was moderately distended without tenderness or rigidity. There was no dulness in the flanks and peristalsis seemed somewhat hyperactive. Shock treatment was instituted and about one-half hour later the blood pressure had risen to 110/80. The abdomen continued to become more distended and peristalsis became entirely inaudible. Moderate generalized tenderness appeared over the abdomen and the walls were felt to become more tense. A flat film of the abdomen, taken at this time, was negative. It was our impression that the patient had suffered a mesenteric thrombosis and an operation was decided upon as soon as he had responded to the shock treatment that had been instituted.

Operation.—May 16, 1939 (N. S. R.): Under ether anesthesia, an upper right rectus incision was made into the peritoneal cavity. A considerable amount of blood exuded. It was dark in color and apparently free of any stomach or intestinal contents. The blood was gradually, and slowly, removed. In excess of 1,000 cc. of blood was aspirated and considerably more was lost from the wound primarily. The abdominal wound was enlarged to obtain a better view.

Operative Pathology.—The mesentery of the small bowel showed no point of bleeding. Examination of the omentum showed no evidence of bleeding. The stomach (only the pyloric and fundal portions could be examined) showed no evidence of a bleeding point. The duodenum appeared normal. There was no evidence of bleeding from the liver, although there seemed to be just as much blood immediately below the liver as there was in the pelvis. The spleen appeared intact and gave no evidence of bleeding in or about it. With practically all of the blood in the peritoneal cavity removed, and inspection revealing no bleeding point or site of continued oozing, the abdomen was closed with through and through silkworm sutures, without drainage. The skin was closed with silkworm gut. During this extensive exploration, the patient went into

deeper shock, despite the fact that intravenous administration of glucose and saline, acacia and blood were administrated during the operative procedure.

Postoperative Course.—Postoperative recovery proceeded uneventfully with the exception of abdominal distention, for which more or less continual duodenal suction syphonage (Wangensteen) was maintained. It was found necessary to keep the Wangensteen apparatus attached and tube suction continued for about 15 days, during which time there was, of necessity, a deficiency in protein and vitamin intake. On June 6, 1939, moderate anasarca appeared with bilateral hydrothoraces and abdominal ascites. The R.B.C. count just prior to this time was 3.1 million, with 55 per cent hemoglobin. Although the total plasma protein was at the lower limits of normal, 6.45 grams per cent, it was felt that some of this represented hemoconcentration from dehydration and that the status of the patient represented primarily an advanced degree of postoperative nutritional and vitamin deficiency. Following paracentesis of sanguineous-tinged effusions from both pleural sacs and from the abdomen, a high protein and vitamin diet was instituted, forti-

TABLE I

ESSENTIAL DATA IN 20 CASES OF INTRA-ABDOMINAL APOPLEXY

Case No.	Author	Year	Sex	Age	Anatomic Location	Cardiovascular System	Operation	Result	Autopsy
1	Barber[2]	1909	F.	32	No definite bleeding point	Apparently normal	Yes	Rec.	—
2	Churchman[3]	1911	M.	48	No definite bleeding point	Apparently normal	Yes	Died	No
3	Florence & Ducuing[4]	1913	F.	—	Sup. mes. art.	—	No	Died	Yes
4	Hilliard[5]	1918	M.	48	N.D.B.P.—(transmesocolon)	Hypertension 160–190 (systolic)	Yes	Died	No
5	Starcke[6]	1923	M.	60	Gast.-duo. art.	Hypertension 155	Yes	Rec.	—
6	Budde[7]	1925	M.	27	L. gast.-epip. art. (aneurysm)	Normal	Yes	Rec.	—
7	Green & Powers[8]	1931	F.	54	L. gast. art.	Hypertension 270/145	Yes	Rec.	—
8	Morgue-Molines & Cabanac[9]	1933	M.	56	L. gast. art.	(Questionable)	Yes	Rec.	—
9	"	1933	—	—	L. gast. art.	Art.-sclerosis & hypertension 230/130	Yes	Rec.	—
10	" (Case of Rud's)	1933	F.	73	L. gast.-epip. art.	Marked art.-sclerosis at P.M.	Yes	Died	Yes
11	Hartley & McKechnie[10]	1934	M.	31	No definite bleeding point	Apparently normal	Yes	Died	Yes
12	Thompson & Dunphy[11]	1935	F.	62	L. gast. art.	Hypertension 170/100	Yes	Rec.	—
13	Buchbinder & Greene[12]	1935	M.	57	R. gast. art.	Hypertension 190/115	Yes	Rec.	—
14	Moorehead & McLester[13]	1936	M.	44	R. & L. gast. art.	Hypertension 220/140	No	Died	Yes
15	"	1936	M.	50	Sup. mesen. art.	Myocardosis with arteriosclerosis	No	Died	Yes
16	Bruce[14]	1937	M.	34	No definite bleeding point	Apparently normal	Yes	Rec.	—
17	"	1937	M.	75	Mid. colic art. (aneurysm)?	Abdominal vessels normal	—	—	—
18	Morton[15]	1938	M.	72	Sup. mes. art.	(Questionable) B.P. 100/70—155/96	Yes	Rec.	—
19	Silverstone[16]	1938	M.	52	No definite bleeding point	Hypertension 200	Yes	Died	—
20	Berk, Rothschild & Doane	1939	M.	52	No definite bleeding point	Hypertension 250/160. Myocardosis & art.-scler.	Yes	Rec.	—

fied by several repeated blood transfusions and daily administrations of vitamin concentrates. Under this regimen the patient made a slow but steady improvement. He was finally permitted out of bed on July 5, 1939, and was discharged in fairly good condition on July 12, 1939.

Follow-up.—The patient was last seen again on October 1, 1939. He had had no digestive disturbances and was free of all abdominal complaints. Since his discharge he had about four attacks of paroxysmal nocturnal dyspnea. He was ambulatory and his color and nutrition were good. His temperature was 97° F., pulse 76, respirations 20, blood pressure 250/160. As noted on earlier examinations, the heart was enlarged. There was a presystolic gallop and a systolic murmur at the apex and base. The aortic second sound had a tambour quality and the pulmonic second sound was split. Ophthalmoscopic examination revealed an hypertensive retinopathy, Grade III. These findings were exactly similar to those on admission and discharge from the hospital.

COMMENT.—An analysis of the 20 cases of intra-abdominal apoplexy, tabulated in Table I, reveals some interesting points. The accident occurred much more frequently in males, with the ratio of occurrence approximately three males to one female. The ages varied from 27 to 73, but the average age was 51.5 years, with the greatest frequency of occurrence between the ages of 45 to 55 (Table I).

Ten cases (50 per cent) gave evidence at some time or other of a definite hypertension. Two other cases, or 10 per cent, in which no blood pressure reading was noted, were described as showing marked arteriosclerosis at postmortem examination. Thus, 60 per cent of the cases in this series presented evidence of organic cardiovascular disease in the nature of a diffuse vascular sclerosis (Table II).

TABLE II

SUMMARY OF ANATOMIC FINDINGS IN 20 CASES OF INTRA-ABDOMINAL APOPLEXY

Cardiovascular Changes				Definite Bleeding Point					No Definite Bleeding Point				
Hypertension		Arteriosclerosis		No. of Cases	Per Cent	Average Age	Normal C-V System		No. of Cases	Per Cent	Average Age	Normal C-V System	
No. of Cases	Per Cent	No. of Cases	Per Cent				No. of Cases	Per Cent				No. of Cases	Per Cent
10	50	2	10	14	70	56.5	1	7	6	30	41.5	4	66.6

In six cases (30 per cent) it was specially noted that no definite bleeding point could be found. It is of interest that these cases occurred among the younger individuals—the average age of this group being 41.5 years compared with 56.5 years in the group in which a definite bleeding vessel was found. In four of these six cases (66 2/3 per cent) the cardiovascular state was noted as being apparently normal (Table II). To state it another way: Of the five cases in the reported series in which it was definitely noted that the cardiovascular state was apparently normal, there were four cases (80 per cent) in which no definite bleeding point could be found either at operation or at postmortem examination. This close association between a younger-age occurrence, a relatively normal cardiovascular apparatus and the inability to demonstrate a bleeding point was striking and noteworthy. The practical

implication of this association becomes apparent when the operative results are analyzed.

Sixteen of the 20 cases in the series (80 per cent) came to operation (Table III). Of these 16, 11 cases (69 per cent) recovered. Of the five (31 per cent), in which operation resulted in death, four were cases in which no definite bleeding point could be found. It would seem from this, that despite the occurrence of a massive intraperitoneal hemorrhage if, at opera-

TABLE III

SUMMARY OF OPERATIVE RESULTS IN 20 CASES OF INTRA-ABDOMINAL APOPLEXY

Operated		Recovered				Died			
				No Def. Bl. Pt.				No Def. Bl. Pt.	
No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases	Per Cent
16	80	11	69	1	9	5	31	4	80

tion, a definite bleeding point can be located and the bleeding vessel ligated, the chance of recovery is excellent. This is especially to be emphasized, since we have been unable to find any reported case of repeated occurrence of intra-abdominal apoplexy. Thus, it would appear that in this condition there might be some advantage favoring the hypertensive-arteriosclerotic individual, in that such patients are much more likely to present a definite bleeding point that would permit of ligation.

In no instance was a correct diagnosis made prior to operation. The majority of cases were felt to represent perforated peptic ulcers. Of the various diagnoses made, the one which would seem most nearly related to the actual condition found was "mesenteric thrombosis." In our case the latter was the preoperative diagnosis. All cases were considered as acute abdominal catastrophes, but in every instance the encountering of an abdomen full of blood occurred as a distinct surgical surprise. A close analysis of the symptoms and signs in each of the reported cases reveals no one thing pathognomonic of the condition. There seems little, if anything, that can be recognized with any degree of certainty, to distinguish it from other acute abdominal emergencies. Of course, the absence in the history of such gross things as trauma, dominant digestive complaints, or previous similar occurrences, are of some aid in the differential diagnosis.

Morridor and Olivier,[1] in their exhaustive review of spontaneous hemoperitoneum in men, resulting from various causes, call attention to several signs and symptoms that were common to most of the cases. They all showed abdominal signs of peritoneal irritation, an elevated leukocyte count (over 10,000 in most cases), and a lowered erythrocyte level.

The quantitative status of the erythrocytes calls attention to the usefulness, in these cases, of recognizing that the clinical picture of vascular collapse which they present is due to internal hemorrhage rather than to shock from other causes. Moon[18] has called attention, on many occasions, to the significance of hemoconcentration as a diagnostic finding in true shock. A

demonstration of hemoconcentration by either repeated hematocrit readings, specific gravity determinations, hemoglobin determinations, or red blood cell counts would indicate a state of shock due to causes other than hemorrhage, whereas the failure to demonstrate hemoconcentration by the same means might suggest hemorrhage as a causative factor. Such a differentiation would appear to be of paramount importance in cases of spontaneous hemoperitoneum, where the most frequent condition, suspected clinically, is ruptured peptic ulcer with shock and, not in a single instance, internal hemorrhage.

There was noted in several of the cases, including our own, a phenomenon, to which Morridor and Olivier[1] have also called attention, namely, that a number of these cases described the occurrence of indefinite abdominal pain of variable nature prior to the acute accident for which they were eventually seen. They, in fact, found that about 25 per cent of the cases which they reviewed, described such pains months or years preceding the acute attack. They also described what they termed "treacherous calm" in about 20 per cent of their cases during which, in a few instances, clinical remissions were so great as to permit return to work.

The use of abdominal paracentesis as a diagnostic procedure in the presence of suspected hemoperitoneum has been recently reapplied by Johnston.[19] Despite the indifferent success of others who have employed the procedure in the past, Johnston feels that the danger of visceral injury is negligible and that exploratory abdominal puncture with the use of a trocar can be of inestimable value in the diagnosis of hemoperitoneum.

The etiology of the condition affords much interesting speculation. The high incidence of hypertension and arteriosclerosis in the reported series of cases (60 per cent) would strongly suggest that local disease of the blood vessels must be the basic, underlying factor. The recent report of Morlock[17] would tend to substantiate such a conclusion. He was able to demonstrate that the blood vessels of the gastro-intestinal tract of hypertensives of all ages as compared to normal individuals, showed measurable thickening of the arteriolar wall and reduction of the ratio of wall to lumen. There occurred early in such blood vessels, hyperplasia of the nuclear elements of the media followed later by degeneration and fibrosis. It is much more difficult to account, on the same local vascular disease basis, for the hemorrhages occurring in the younger individuals with an apparently normal vascular tree. The close association was pointed out above of a younger-age occurrence, the presence of an apparently normal vasculature, and the inability to demonstrate a definite bleeding point (Table II). Bruce,[14] discussing the cause for intra-abdominal apoplexy, suggested the presence in the abdominal vessels of a congenital weakness, similar to that which leads to aneurysm of the basal cerebral arteries. He quoted the work of Forbus, whose study on the development of the mesenteric vessels indicated that at the branchings of the arterial tree a gap exists temporarily between the independent formation of muscle coats on each branch. It was felt that developmental defects at the branchings, resulting from deficiency in the formation of muscle coats, might

explain the occurrence of small aneurysmal formations. Small aneurysmal dilatations, similar to that seen in cerebral arteries, have been reported in the mesenteric, pulmonic and renal arteries. Such conditions would lend an easy explanation for the occurrence of a massive intraperitoneal hemorrhage in younger individuals, free of known organic vascular disease. There is, of course, no sure proof that such a condition actually exists, but the demonstration of small aneurysmal rupture in Cases 6 and 17, where the surrounding abdominal vessels were noted to be normal, would lend support to such a theory.

The spontaneous feature in all these cases of intra-abdominal apoplexy is an important one. The precipitating cause is, in most instances, hidden and unexplainable. Given a basic, underlying local disease or congenital defect whose very nature is such as to weaken the vessel at the local site, then the addition of anything that would tend to raise the intravascular pressure within that vessel might well result in a rupture at the weakened site. In that way, and for that reason, hypertension, possibly, is found in so large a percentage of cases. Likewise, too, the use of pitressin, as in Morton's[15] case, sudden emotional strain, excessive eating, coitus, heavy lifting, and anything else which might raise the blood pressure could well predispose to a "blowing out" of a blood vessel.

Summary

(1) A case of massive spontaneous intra-peritoneal hemorrhage ("intra-abdominal apoplexy") is reported.

(2) Nineteen similar cases reported in the literature are analyzed.

(3) The striking features of the condition are noted, and a discussion is made of the possible etiology, the treatment and its results.

Conclusions

(1) Massive spontaneous intraperitoneal hemorrhage resulting from the nontraumatic rupture of a small intra-abdominal blood vessel (so-called "intra-abdominal apoplexy") is a rare condition, the occurrence of which is being reported with greater frequency.

(2) There is nothing pathognomonic in either the symptoms or signs that permit a certain preoperative diagnosis.

(3) The condition should be considered in all cases in which there occurs sudden severe abdominal pain, shock, and signs of peritoneal irritation especially in a known hypertensive.

(4) Hypertension and arteriosclerosis seem to be the dominant factors in the etiology of the condition. The possibility of the occurrence of small localized aneurysmal dilatations, particularly in younger individuals, has been suggested.

(5) Early operation, with ligation of the bleeding point, if possible, is the only treatment. This treatment is one which offers a high chance of recovery if a definite bleeding point be found.

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INTRACTABLE GASTRIC ULCER WITH FINAL MALIGNANT CHANGE ASSOCIATED WITH A BENIGN TUMOR OF THE BRAIN*

P. H. T. Thorlakson, M.D., F.R.C.S. (C.)

AND

Sarah Meltzer, M.D.

Winnipeg, Canada

During the past ten years our whole attitude toward the problem of gastric and duodenal ulcer has undergone a radical change. Formerly, the diagnosis and treatment of gastric or duodenal ulcer directed attention chiefly to the local lesion and largely ignored constitutional factors, which we now know to be of fundamental importance. At present, ulcers are believed to be due to a combination of factors acting in a susceptible individual.

The two opposing conceptions of the etiology of ulcer have contended for first place for many decades: First, the view suggested by Rokitansky, in 1841, that some central factor is the real cause of all ulcers; second, the view upheld by Virchow, in 1853, that local factors are quite sufficient to explain the pathogenesis of ulcer.

Undoubtedly both the central and the local factors are important but the accumulating evidence suggests that central factors, either in the nature of organic disease of the brain, or neurogenic stimuli from the cortex in a vagotonic type of individual, are fundamental or predisposing causes of peptic ulceration.

The local factors which are of significance will merely be enumerated here. They are: Trauma; acid chyme erosion; and bacterial invasion. These factors are of importance, but it is probable that their effect is secondary to the preexisting central disturbance. Alterations in the gastric motility and secretion and actual peptic ulceration may be produced by stimuli originating in higher centers.

The view one takes as to the relative importance of the central or local group of factors will influence one's line of treatment. If the predominant factor in a given case is central—that is to say due to either a functional or organic cerebral disturbance—and it cannot be satisfactorily controlled, then any form of local surgical therapy is apt to be followed by early recurrence of the ulcer. In this type of case medical treatment should be persisted with. However, if for any reason operative interference becomes necessary, a radical procedure must be adopted. On the other hand, if the central factors are negligible or controllable, and the local factors predominant, then medical treatment or conservative surgery offers the patient a much greater chance of cure.

* Read at the Annual Meeting of the Canadian Medical Association, Montreal, June, 1939. Submitted for publication November 24, 1939.

The growth of the neurogenic hypothesis has been slow since it was originally suggested by Rokitansky. The evidence on which it is based is threefold: First, the existence of cerebral lesions and peptic ulcers in the same

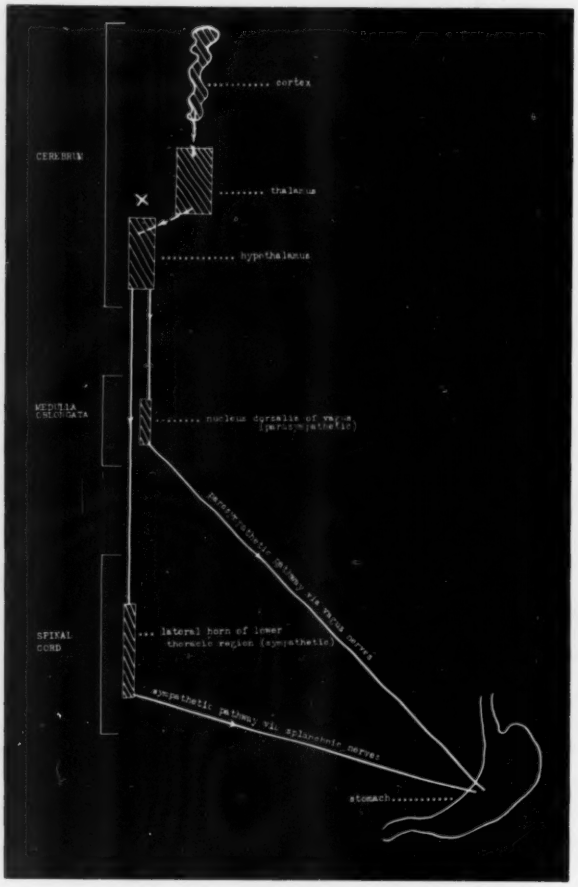

FIG. 1.—A schematic representation of some current ideas regarding nervous control of the stomach. The arrows indicate the direction of controlling impulses. In the diagram pre- and postganglionic fibers and the intervening synapse are not distinguished. The hypothalamus is known to exert some control over both sympathetic and parasympathetic systems; it may coordinate them; but our knowledge of the functional significance of the numerous hypothalamic nuclei is not sufficiently definite to warrant inclusion in such a diagram. There is good evidence that the nervous apparatus controlling the gastro-intestinal canal includes the cortex; a probable pathway (though not necessarily the only one) through which the cortex affects the hypothalamus .(via the thalamus) is suggested by broken lines. The X indicates the approximate position of the tumor in our case; it may have affected the hypothalamus itself, or some fibers transmitting controlling impulses to the hypothalamus.

We are indebted to Dr. I. M. Thompson, Professor of Anatomy, University of Manitoba, for the diagram illustrating the nervous control of the stomach.

individual; second, the occurrence of peptic ulceration in infants following cerebral injury; third, there is considerable experimental evidence to show that induced vagal and sympathetic disturbances will produce ulcer in animals,

not to mention the production of ulcer from stimulation or injury of cortical areas.

Cerebral Lesions and Peptic Ulcer.—Hoffmann,[9] in 1868, had a patient under observation who had a tumor of the pons and medulla. The patient died of perforated gastric ulcer. Arndt,[10] in 1874, reported a patient with an interpeduncular sarcoma who developed a fatal gastric ulcer. von Winiwarter,[11] in 1911, recorded two cases of fatal gastric hemorrhage following a brain operation. Beneke,[12] in 1908, found that 70 patients out of 239 with fatal gastric hemorrhage had associated intracranial lesions. Mogilnitsky,[5] in 1925, reported eight cases of brain tumor who had peptic ulcers. Cushing,[8] in 1932, reported 11 cases of intracranial lesions with associated gastric or duodenal ulcer.

Ulcers and Intracranial Injury in the Newborn.—The extreme rarity of peptic ulcer in infancy in the absence of intracranial lesions, and the comparative frequency with which ulcers are found in association with brain injuries in the newborn suggest an etiologic relationship between brain lesions and ulcer. von Preuschen[13] recorded a case of intracranial hemorrhage and gastric erosion. von Preuschen and Pomorski[14] performed a number of experiments upon animals in which they injured the hindbrain and produced gastric erosion. Blackfan[20] recorded four cases of esophageal perforation in the newborn, and in all of these patients intracranial hemorrhage was present.

Experimental Neurogenic Ulcer.—The sympathetic and parasympathetic nervous systems together constitute a balanced mechanism as far as gastric motility and secretion are concerned. Experimental attack on the vagus or the sympathetic may result in gastric ulceration. Theoretically, division of the vagus should not produce gastric ulceration. Actually, however, ulcers have been produced by this procedure. Manning, Hall and Banting,[3] in 1937, showed that prolonged vagal stimulation would give rise to areas of hemorrhage and congestion in both pylorus and duodenum. Atropine prevented such lesions, while eserine accentuated them and resulted in ulcer formation. Division of the sympathetic pathways to the stomach gives rise to an uncontrolled vagus action. Gastric erosions and ulcerations have been recorded by a number of observers following section of sympathetic nerves to the stomach.

Schiff[15] showed that stimulating the vagus via the higher centers, namely, the hypothalamus, gave rise to dilatation of the vessels in the stomach musculature. On the other hand, stimulation of the sympathetic through the higher centers resulted in constriction of the vessels in the stomach mucosa and in decreased peristalsis. Ebstein[16] injured the anterior corpora quadrigemina and produced ulcers in nine out of 23 experimental animals. Burdenko and Mogilnitsky,[6] in 1925–26, punctured the hypothalamus and, as a result, obtained gastric erosions and perforations and in some instances chronic gastric ulcers.

Pharmacologic Investigations.—Eppinger and Hess,[17] in 1910, showed that certain individuals may be described as vagotonic, and that this type of individual is susceptible to ulcer formation. These people react excessively to

certain vagal stimulating drugs, such as pilocarpine and physostigmine. In 1914, Westphal[18] showed that subcutaneous injections of pilocarpine or physostigmine in experimental animals gave rise to ulcer if the stomach contained acid and was digesting food at the time of the injection. Ettinger, Hall, and Banting,[4] in 1936, found that by repeated intravenous injections of acetylcholine in dogs, the younger animals developed severe congestion of the gastric and duodenal mucosa. Clinically, this was manifested by retching, vomiting, diarrhea, and melena. Older animals showed a lesser tendency to develop these gastro-intestinal lesions; instead, they developed marked changes in the coronary vessels.

Light, Bishop, and Kendall[19] introduced into the ventricles of the brain pituitrin and pilocarpine in small doses, and were able to produce gastric erosions similar to those resulting from vagus stimulation. Their experiments suggested that the vagus has a controlling center situated in the diencephalon. Roentgenographic and chemical examination of the stomach in experimental animals, following the intramuscular and the intraventricular injection of pituitrin, pilocarpine and histamine, show hypermotility, hypertonicity, and hyperchlorhydria. All of these abnormalities are commonly present in chronic gastric or duodenal ulcer.

The appended case report is presented for three reasons: First, because it demonstrates an apparent causal relationship between an intracranial lesion and a chronic gastric ulcer; second, because this gastric ulcer failed to respond to any form of treatment, possibly due to the persistence of the intracranial lesion; and finally, the ulcer developed malignant change. As far as we are able to ascertain this is the first case to be recorded of an ulcer with such a definite intracranial lesion which has ultimately developed a gastric carcinoma.

Case Report.—Hosp. No. A-3207: G. W., female, age 34, unmarried, was admitted to the Winnipeg General Hospital, in February, 1923, suffering from almost continuous occipital headaches, poor sight, loss of memory, irritability, and nervousness. She dated her illness back to April, 1922. Her first symptom was headache which became increasingly severe, awakening her at night. The headaches became progressively more severe, and in the summer of 1922 she started to have periodic attacks of vomiting. The vomiting was never projectile, and was preceded by nausea. In December, 1922, she was placed on a milk diet for five or six weeks, with relief of epigastric distress and nausea. Six months after the onset of the headaches she consulted an oculist because of failing vision.

Physical Examination showed dilated pupils reacting to light and accommodation, right nasal hemianopsia, and great reduction in the visual fields of both eyes. The disks were choked and there were retinal hemorrhages. Reflexes were all present and active, there were no changes in sensation, coordination was good, and there was no ataxia. A lumbar puncture at that time showed a pressure of 40 Mm.Hg. There was no abnormality in the spinal fluid. A roentgenogram of the skull showed partial absorption of the posterior clinoid process on the right side. At this time she became totally blind. Following ventriculography, there was vomiting of clear fluid, but no mention was made of epigastric pain or of blood in the vomitus. The ventriculogram suggested a midline shift of the third ventricle to the right, with no deformity of the lateral ventricles.

In April, 1923, the first craniotomy was performed by Dr. O. S. Waugh: The exploring needle encountered a firm, resistant mass in the suprasellar region at a depth

of about 6 cm. A left subtemporal decompression was accomplished. Following this there was marked improvement in her general condition, and her sight returned so that she was enabled to go on tour with a theatrical troupe.

Her second admission was in September, 1924. She now had repeated convulsions, with jerking movements of the left side of the body. Spinal fluid pressure was now 18 Mm.Hg. The original left-sided subtemporal decompression had completely filled in with bone. Bilateral subtemporal decompressions were now performed. There was a great tendency for these decompressions to regenerate bone and become solid. As they filled in, her symptoms returned. Finally, permanent openings were obtained, which resulted in a marked amelioration of her cranial symptoms.

Subsequent Course.—Although this patient had previously complained of epigastric distress following certain articles of diet, these symptoms were overshadowed by the neurologic manifestations. In October, 1929, however, she was readmitted to the hospital because of severe, constant epigastric pain, which had been present for one year, associated with flatulence, vomiting, and some loss of weight. Gastric analysis revealed no increase in free hydrochloric acid. A roentgenogram showed a perforating ulcer on the lesser curvature of the stomach near the cardia. In November, 1929, the ulcer was excised and it was reported by Dr. William Boyd as an innocent one.

In April, 1935, she was again admitted to the hospital, complaining of gaseous indigestion of three years' duration, and regurgitation of food. Roentgenograms showed hour-glass deformity but no ulcer crater. There was no improvement on a Sippy regimen; a posterior gastro-enterostomy was performed, which resulted in some improvement of her symptoms.

In October, 1937, she was again admitted to the hospital, complaining of epigastric pain two hours after meals, relieved by food. Gastric analysis was normal. Roentgenograms showed a large crater on the lesser curvature and an hour-glass deformity.

This patient came under observation first in July, 1938. The ulcer symptoms had increased, and the stools were positive for occult blood. There was no improvement with therapy which included a feeding jejunostomy. A large gastric ulcer on the lesser curvature proximal to the gastro-enterostomy stoma was demonstrated with the gastroscope. The patient went progressively downhill, vomiting, losing weight, and becoming very weak, until her death in October, 1938. For the last ten years her central nervous complaints had cleared up, apart from marked impairment of vision and occasional epileptic seizures which were readily controlled by luminal.

Autopsy.—The body was that of a small, extremely thin woman, 34 years of age. There was a deficiency in the skull in the temporoparietal region on each side. There were arachnoid adhesions in these areas. The brain showed no abnormality on the external surface. There was no evidence of increased intracranial pressure. On opening the brain, a rounded, firm tumor, 2.5 cm. in diameter, was found in the right frontal lobe immediately anterior to and encroaching on the anterior portion of the corpus callosum and the mesial surface of the lobe, and pushing the medial surface of the frontal lobe across the median plane to the left. It was invading the junction of the body and the anterior horn of the lateral ventricle. It passed down through the corpus callosum, encroaching on the septum lucidum, fornix, and the head of the caudate nucleus. The lamina terminalis of the third ventricle was compressed. The inferior horn of the lateral ventricle was dilated. On section, the tumor was firm, smooth, and pinkish in color, with irregular cystic spaces. Microscopically, it was a fibrillary astrocytoma.

There were numerous dense adhesions in the upper abdomen. The stomach showed a large ulcer on the lesser curvature and anterior wall, 2 cm. in diameter. It was sharply defined with a smooth base and rounded edges. There were no enlarged lymph nodes. Microscopically, the picture was that of a very chronic peptic ulcer with malignant changes at one edge. The epithelial cells here were of the signet-ring type, and there was mucin in the stoma. No metastases were found in any of the organs.

FIG. 2.—The tumor in the right frontal lobe pressing on the genu of the corpus callosum.

FIG. 3.—Showing the deepest portion of the tumor encroaching on the fornix and lateral ventricle.

FIG. 4.—Showing the large ulcer on the lesser curvature and anterior wall.

SUMMARY

A striking case is recorded of a woman who suffered from an intracranial tumor in 1923, and who developed a gastric ulcer which recurred on several occasions, after various forms of medical and surgical treatment. At autopsy, a fibrillary astrocytoma was found in the right frontal lobe encroaching on the corpus callosum, the lateral ventricle, septum lucidum, fornix and lamina terminalis of the third ventricle. The ulcer showed beginning malignant change.

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GIANT DIVERTICULUM OR DUPLICATION OF THE INTESTINE WITH RECURRENT PERFORATIONS

JOHN W. DUCKETT, M.D.
DALLAS, TEX.

A LARGE GROUP of anomalies consisting of cysts and diverticula whose walls show the same histologic structure as the alimentary tract may, for the sake of simplicity, be regarded as duplications of the alimentary tract. They are possibly the results of abortive attempts at twinning, or they may have had their origin in the so-called "nodules of Lewis and Thyng."[8] This group, however, must be differentiated from the true Meckel's diverticulum.

The indiscriminate use of the term "Meckel's diverticulum," as applied to all diverticula of the lower ileum, is an unfortunate custom. It is true that most diverticula found in this region are situated on the antimesenteric border of the intestine and probably *are* the unobliterated remnants of the vitelline duct, thus fitting appropriately Meckel's[1] original description. There are some diverticula, however, usually but not always of the lower ileum, which are located on the opposite side of the intestine, lying wholly or in part between the leaves of the mesentery; and it seems certain that these have an entirely different origin. They are, undoubtedly, congenital, since they often give rise to symptoms early in life, have structure similar to that of the intestinal tract, and show evidences of heterotopia. They are often very large, and may cause serious symptoms. Many, however, are symptomless, as shown by their incidental discovery at operation or autopsy.

The following case is reported because of its unusual and dramatic clinical features, and because it contributes forcible evidence to the view that such intramesenteric diverticula are not Meckelian in origin.

Case Report.—E. A. M., a white, female child, three and one-half years old, was brought by her parents to the hospital in Shawnee, Oklahoma, August 29, 1938, consulting Dr. F. L. Carson. She was acutely ill, suffering from severe generalized abdominal pain, which had begun suddenly on the preceding evening, and had been accompanied by frequent vomiting. For the three days preceding the onset of pain and vomiting, she had passed numerous black tarry stools, and had become weak and pale.

It was recalled that, at the age of six weeks, she began to pass tarry stools and to cry, as if in abdominal pain. This episode lasted six weeks, after which she was well until the age of 18 months, when she developed a purpuric eruption over the body and lower extremities. After blood transfusion, the eruption disappeared and she remained well until the present illness, although somewhat frail and underweight. Both parents and an older sister were normal and healthy.

Physical Examination.—The patient presented the picture of shock, with extreme pallor, cold skin, rapid, thready pulse, and a diffusely tender abdomen, rigid in the lower half, where an indistinct mass could be felt. Blood count showed hemoglobin 40 per cent; red cells, 2,500,000. Urine was normal. *Clinical Diagnosis:* Peptic ulcer of Meckel's diverticulum with perforation.

Submitted for publication August 27, 1939.

Because of the dangerous general condition, supportive treatment was administered, including a blood transfusion, and operation delayed until the following day.

First Operation.—August 30, 1938: Doctor Carson. Under ether anesthesia, a low right rectus incision was made; and, when the peritoneum was opened, a gush of bloody fluid and gas was encountered. There were extensive fibrinous adhesions everywhere, but rapid exploration revealed the site of a perforation in the ileum near the ileocecal valve, as well as could be determined. There was no well-developed diverticulum seen, but a definite bulge of the antimesenteric border of the ileum, with the perforation at its apex, was found. The fluid contents of the abdomen were aspirated; the perforation

FIG. 1.—Drawing of diverticulum and adjoining ileum as seen at second operation. The perforation is shown near the base of the fibrous remnant of the omphalomesenteric duct.

closed with a purse-string suture; and the wound closed in layers, with one cigarette drain inserted.

After a stormy convalescence, the child recovered and the wound was healed in about four weeks. Stools became normal in appearance. Appetite improved and she began gaining weight.

On November 24, 1938, three months later, while the patient and her parents were visiting in Dallas, Texas, she became suddenly ill again with severe pain in the lower abdomen, followed by vomiting and circulatory collapse. The parents recognized the signs as a recurrence of the previous catastrophe and promptly called Dr. G. L. Hacker, who had her taken to the Baylor University Hospital. The abdomen was again found

to be rigid and the diagnosis not to be doubted, but treatment for shock was imperative before operation could be attempted. After administering morphine sulfate gr. 1/16 and adrenalin chloride solution 0.5 cc., followed by 5 per cent glucose, 200 cc., intravenously, and a transfusion of citrated blood, 200 cc., the child's condition improved; and operation was performed about six hours after onset of symptoms. Hemoglobin 48.6 per cent; R.B.C. 2,760,000; W.B.C. 16,650; bands 30 per cent; segmented neutrophils 46 per cent. Urinalysis: Specific gravity 1.028, acid, albumin trace, acetone 4 plus.

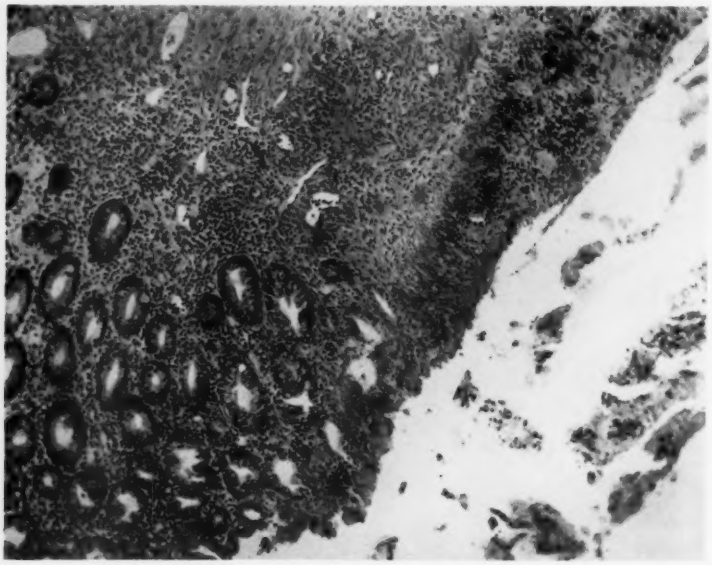

FIG. 2.—Photomicrograph of section at edge of perforated ulcer, showing characteristic intestinal mucosa.

Second Operation.—November 25, 1938: Doctor Duckett. Under ethylene and ether anesthesia, a suprapubic midline incision was made. There was again peritonitis present, and a perforation in the ileum, but this time on the lateral wall. It could now be seen that no ordinary Meckel's diverticulum was present, but between the leaves of the mesentery, and lying parallel to the ileum, was an elongated diverticulum or reduplication of the ileum. This tube-like structure was approximately 30 cm. long, of about the same diameter as the adjacent intestine and, at its midpoint, communicated through a wide opening with the lumen of the intestine exactly at the site of perforation. Near the antimesenteric border of the ileum, close to the perforation, originated a fibrous cord, 5 Mm. in diameter, which looped over and behind the ileum to be attached at its other end to the base of the mesentery on the opposite side (Fig. 1).

It was apparent that removal of the diverticulum would be impossible without great risk to the child's life. Resection of the diverticulum, because of its close proximity to the ileum, would have undoubtedly jeopardized the blood supply of the ileum. Resection of the diverticulum and ileum was too extensive a procedure for the child to tolerate under the existing circumstances. Closure of the perforation was the only recourse, but this proved to be a difficult problem because of the thickness and friability of the wall at the junction of the ileum and diverticulum. Because of the ample space provided, and the large opening between ileum and diverticulum, an elliptical excision of the perforated ulcer was made, leaving fairly normal intestinal wall at the sides of the defect, which were sutured together with inverting mattress sutures of fine chromic catgut. The fibrous cord, previously described, was also removed with this section of the ileal wall, being cut at

its point of attachment to the mesentery. The fluid contents of the abdomen were aspirated, and the wound closed in layers without drains.

A very satisfactory postoperative course followed and, after several transfusions, the child left the hospital on the tenth postoperative day. Blood count: Hemoglobin 107 per cent; R.B.C. 5,700,000. Stools showed a few red blood cells only.

Pathologic Examination.—Microscopic: "The bowel wall shows a mucosa which contains numerous slightly tortuous tubular glands lined by simple columnar epithelium of the goblet cell type. In some areas, these glands appear distorted. The stroma between these glands contains a diffuse infiltration of plasma cells, eosinophils, lymphoid cells, and occasional polymorphonuclear neutrophils (Fig. 2). The submucosa contains a similar type of exudate.

"At one point, there is an ulceration extending through the entire bowel wall. Adja-

FIG. 3.—Photomicrograph of section of fibrous remnant of omphalomesenteric duct.

cent to this area of ulceration, there is dense fibrous tissue in all layers of the wall, most marked in the subserous layer. The superficial layers are necrotic and contain much fibrin. On the outer surface of the adjacent bowel wall, there are many polymorphonuclear neutrophils in various stages of disintegration. A large amount of fibrin is also present and tissues stain poorly with a granular appearance. No gastric mucosa is seen.

"Sections of the cord-like structure show dense fibrous tissue with a few plasma cells and lymphoid cells, and a few small thick-walled blood vessels (Fig. 3). *Pathologic Diagnosis:* Acute inflammation in a chronic ulcer at junction of ileum and bifurcated diverticulum. Acute necrotizing peritonitis."

The child was allowed to go to her home in Oklahoma for convalescence, but it was planned for her to return to Dallas after six to eight weeks for resection of the diverticulum, if her condition was favorable. After two weeks at home, however, she began to have recurrence of abdominal pain and tarry stools, both of which were of daily occurrence. She was, consequently, brought back to Dallas and readmitted to Baylor University Hospital, January 4, 1939, for operation. Temperature 101° F., pulse 100, respirations

26. Hemoglobin 72 per cent; R.B.C. 4,350,000; W.B.C. 11,900, bands 33 per cent, segmented neutrophils 38 per cent. Urine was normal.

Third Operation.—January 5, 1939: Doctor Duckett. Under nitrous oxide–ethylene-ether anesthesia, the scar of the previous low right rectus incision was excised and the peritoneum opened. The loop of ileum with the adjoining diverticulum, previously described, was easily located and delivered through the wound. The wound in the intestine and diverticulum made at the previous operation was well healed but there was some constriction of the ileum at this point. There were signs of a low grade peritonitis, all

FIG. 4.—Photograph of resected diverticulum and adjoining ileum: (A) intact, (B) opened at middle orifice.

peritoneal surfaces being moderately red and edematous and, in the mesentery common to the diverticulum and ileum, there were a number of large, firm lymph nodes, the largest measuring 2x1.5 cm. The ileum was traced distally to the ileocecal valve, a distance of 50 cm., where the appendix was inspected and found normal in appearance. It was not removed.

Using a Furniss intestinal anastomosis clamp, a length of ileum 42 cm. long was resected, together with the attached diverticulum and a V-shaped section of mesentery,

including most of the enlarged lymph nodes (Fig. 4). At the proximal end of the diverticulum, the tip was severed and about 1 cm. of the diverticulum was left at the base of the mesentery where its removal might have caused injury to large blood vessels. The mucosa of this tip was completely removed, however. An end-to-end anastomosis was performed over the pin of the Furniss clamp, using a continuous suture of No. 0 chromic catgut reenforced by an overlying row of black silk mattress sutures. The wound was closed in layers without drains.

FIG. 5.—Drawing of diverticulum and adjoining ileum to show communicating openings and small ulcer of the mucosa of the ileum.

Shortly after operation, abdominal distention and vomiting developed, which were, however, relieved by the Wangensteen duodenal suction, which was used for three days. One blood transfusion was administered, in addition to glucose, sodium lactate, and Hartmann's solution intravenously and subcutaneously. On the fifth postoperative day, toast, crackers, and gelatin were well tolerated and, from then on, convalescence was rapid and uneventful. She was discharged, January 19, 1939, 14 days after operation, with the wound healed. Hemoglobin 83 per cent; R.B.C. 4,350,000. Urine normal. There was no blood in the stools.

Pathologic Examination.—Gross: "The specimen consists of 42 cm. of ileum with attached section of mesentery between the leaves of which is a diverticulum 27 cm. long. This diverticulum lies close against the lesser curvature of the resected loop of ileum, and communicates with the ileum both at the middle and at the distal end of the diverticulum. In the fused wall of ileum and diverticulum, at the middle site of communication, is a depressed scar of a previous surgical incision about 4 cm. long (Fig. 5).

"When the walls of the specimens were incised, both ileum and diverticulum were found lined with apparently normal mucosa except for a shallow ulceration in the mucosa of the ileum immediately adjoining the communicating opening at the middle of the diverticulum.

"There was no gross blood found in either lumen. The mucoid secretion in the diverticulum was washed out with a small quantity of distilled water, and was found to have an acidity of 5°.

"Microscopic Study.—Dr. George T. Caldwell, Pathologist-in-Chief: Sections taken from multiple areas in the walls of the ileal segment, and from the diverticulum, showed the ileum to be lined with normal intestinal mucosa, and the diverticulum with normal

gastric mucosa (Figs. 6 and 7). No pancreatic or other aberrant tissues were found, although careful search was made for these anomalies."

Since her last operation, the child has gained weight and strength continuously. She has had three attacks of moderately severe lower abdominal pain, once accompanied by nausea and vomiting, but each attack lasted only a few hours. There has been no return of tarry stools, and a specimen of stool examined May 27, 1939, showed no blood. A gastro-intestinal series, May 26, 1939, showed no sign of obstruction or other abnormality in the stomach or intestines. Barium was seen in large quantity in the cecum four hours after taking the meal. Hemoglobin 75 per cent; R.B.C. 3,750,000.

FIG. 6.—Photomicrograph of section of gastric mucosa lining the diverticulum. (Low power)

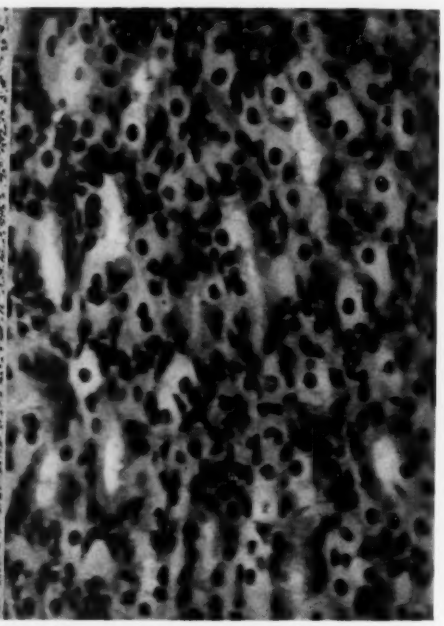

FIG. 7.—Higher magnification of section shown in Figure 6. Note characteristic gastric glands with parietal cells.

COMMENT.—This case is of unusual clinical interest for a number of reasons: The seriousness of the problem offered by such a giant diverticulum is evidenced by the fact that the reports of only six similar cases, successfully operated upon, have been found. Positive diagnosis in the past has been extremely difficult but should be more frequently made since now it is generally recognized that many diverticula contain heterotopic gastric mucosa associated with ulceration and that when this condition is present blood in the stools is a constant finding. Stools are usually tarry but the blood may be fresh, and rectal polypi or other rectal disease must be eliminated as a source of the bleeding. Since this type of diverticulum is always congenital, bleeding from the rectum usually begins in infancy. When perforation of an ulcer in or associated with a diverticulum occurs, the diagnosis is practically unmistakable. Perforation of a gastric or duodenal ulcer may be differentiated by location of the pain in the upper abdomen, and perforation of a typhoid ulcer by recognition of the preceding characteristic febrile illness.

It is further significant that the true nature of the diverticulum was not discovered at the first operation. This was probably accounted for by the fact that the patient's condition was extremely precarious and haste was an essential factor in the success of the operation. The intramesenteric location of the diverticulum made it difficult to recognize, however; and, even if haste had not been necessary, it might easily have been overlooked. Hudson[13] calls attention to this fact in his discussion of giant diverticula, stating that, during the operation upon one of his patients, nearby spectators could see the diverticulum only indistinctly after it was pointed out to them. This emphasizes the necessity for very careful inspection, not only of the intestine itself but also of the mesentery, during exploration to ascertain the etiology of obscure abdominal symptoms.

The technical problem involved in removing a giant intramesenteric diverticulum may present considerable difficulty. Abt and Strauss[2] were able to resect a diverticulum 18 inches long without removal of the adjoining ileum. They state that in their case the blood vessels of the diverticulum were separate and parallel to those supplying the ileum, but in most cases there has been a blood supply common to both, the vessels normally supplying the ileum merely sending off branches to the diverticulum in passing to either side of it. Close apposition of the wall of the diverticulum to that of the intestine may make their separation impossible. The size of the opening between diverticulum and intestine may be too great to allow adequate closure of the defect remaining in the intestinal wall after resection of the diverticulum. All of these factors may be present, as in the case reported herewith; and, consequently, resection of a length of intestine with the diverticulum may be necessary. If at all possible, primary anastomosis, preferably end-to-end, should be performed. These children tolerate very poorly the loss of fluid and the necessity for multiple operative procedure following double-barreled enterostomy. Normark[3] points out that the only operative cases which have recovered were those in which one-stage resection and entero-anastomosis were performed.

In addition to the features of clinical interest, this case is of significance in shedding further light on the probable origin of such intramesenteric diverticula. Since the vitelline duct is an outgrowth of the primitive intestine on the antimesenteric border, it is difficult to consider a structure lying within the leaves of the mesentery as being derived from the duct. Furthermore, in this case, a cord-like structure was found attached at one end to the wall of the ileum near its antimesenteric border, and at its other end to the base of the mesentery. Such cords have been found attached as terminal filaments to the ends of typical Meckel's diverticula. The distal end of the cord may be free, attached at the umbilicus, or attached to the mesentery or other abdominal organ. Cords, similar to this one, have also been described as occurring without diverticula, but from their structure and location are generally regarded as remnants of the vitelline duct and omphalomesenteric blood vessels. It is impossible for two vitelline ducts to occur in the same individual;

hence, the presence of the cord-like remains of the duct and vessels on one side of the intestine make it necessary to assign another mode of origin to the diverticulum on the other side. Similar evidence is found in the case reported by Edwards.[4] A small, but typical Meckel's diverticulum was discovered on the resected intestine and, in addition, an adjoining giant intramesenteric diverticulum. The patient survived.

Using his findings as a basis, Edwards discussed at length the etiology of congenital diverticula of the intestine. He stated that the great majority of congenital diverticula are Meckel's diverticula, but there is a small remaining group whose etiology differs from those of the Meckelian type "in that, whereas Meckel's diverticula result from an arrest of normal development, the others arise as a result of abnormal development." He considers giant diverticula to be true reduplications of the bowel, and to "represent an attempt at the formation of a twin, which has come at a comparatively late stage of development of the ovum, so that the extent of reduplication is limited to a segment of the bowel." Webster,[5] reporting a "Giant Diverticulum (Reduplication) of the Colon" in a child, who also had accessory fingers and toes, suggests that the simultaneous occurrence of these abnormalities indicates that both phenomena represent a mistimed or belated attempt at formation of a twin.

Evans,[6] however, presents strong arguments in favor of another explanation for the development of cysts and diverticula of enterogenous origin, but not of the true Meckel's type. He recalls attention to the "nodules of Lewis and Thyng." These are outgrowths of epithelium from the primitive intestinal canal first described by Keibel,[7] in 1905, but more fully by Lewis and Thyng,[8] in 1907–8. These nodules were found consistently in sections of rabbit, pig, and human embryos. Some were seen to have become vacuolated and to form either cysts or diverticula, depending on whether or not they communicated with the intestinal lumen. In later embryos, the nodules, cysts, and diverticula were scarce or absent, indicating that they became absorbed or coalesced with the developing intestine. Persistence of these primitive cysts and diverticula could readily account for many of the cysts and diverticula found associated with the intestinal tract after birth. Further support for this view is the finding of an intramesenteric diverticulum of the intestine and a mediastinal cyst in the same individual, both diverticulum and cyst having structures typical of the intestinal tract. Such cases have been reported by Roth,[9] Moll,[10] Poucher and Milles,[11] and Black and Benjamin.[12] The statement has been made that the observations of Lewis and Thyng have not been confirmed. Since this seemed strange, the writer obtained serial sections of a 6 Mm. human embryo from the Embryology Laboratory of the Baylor Medical School, and, on examination of these sections, three diverticula similar to those described by these investigators were easily identified. The accompanying reproduction of a photomicrograph shows two of these diverticula at the same level in the small intestine (Fig. 8). Since they are thus readily found, it would seem that the nodules of Lewis and Thyng are

quite real, and offer a satisfactory and logical explanation for the origin of diverticula other than Meckel's.

Hudson,[13] in 1935, published a review of the subject entitled "Giant Diverticula or Reduplications of the Intestinal Tract" with a complete bibliography. He found 18 cases previously reported, and added three. W. E. Ladd,[14] in 1937, reviews the more inclusive subject of enterogenous cysts and diverticula, grouping them together under the term "Duplications of the Alimentary Tract." In order to simplify the confused nomenclature of these conditions, Doctor Ladd refers to them as "cystic duplications," regardless of whether or not the lumen of the anomalous structure has one or more connections with the lumen of the alimentary tract. The essential feature, he

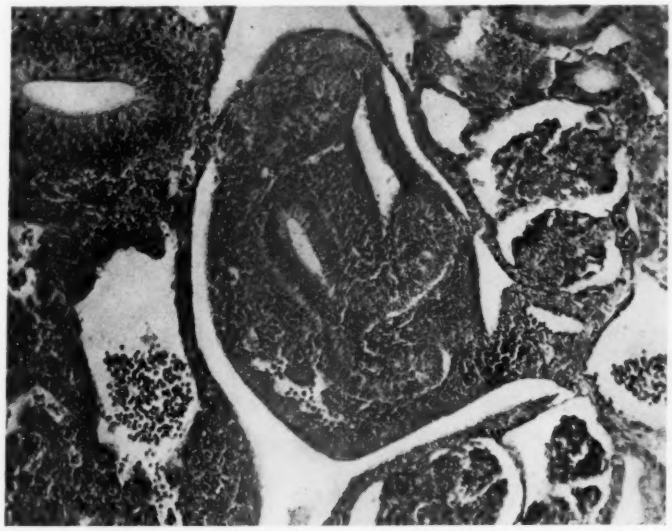

FIG. 8.—Photomicrograph of section of 6 Mm. human embryo showing two diverticula connected with the primitive small intestine. These out-pouchings were traced through adjacent sections in the series and proved, without doubt, to be diverticula.

believes, is the similarity in structure of the walls. Three of his cases, requiring resection and anastomosis, survived.

Until more definite evidence is obtained as to their exact mode of origin, it seems logical to consider these structures as duplications of the alimentary tract. It is entirely a matter of conjecture as to whether they arise from the "nodules of Lewis and Thyng" or whether they are examples of "twinning." In describing these duplications, however, it is necessary to distinguish between cysts and diverticula, since the clinical problems which they present are usually quite different and characteristic.

In addition to the cases from the Boston Children's Hospital reported by Ladd[14] and by Hudson,[13] recent publications contain several similar cases of interest. The one described by Abt and Strauss[2] is unique in that the diverticulum, in an 11-month-old boy, although situated entirely between the leaves of the mesentery, had a separate blood supply, its vessels being parallel to

those supplying the ileum beyond it. The diverticulum was successfully resected without damage to the ileum or its blood supply. The mucosa of the diverticulum showed characteristic structure of intestinal mucous membrane, and there were no ulcerations.

Black and Benjamin[12] in 1936, reported the autopsy findings in an infant five and one-half months old, which included an enterogenous intestinal pouch or diverticulum, 10 cm. long, lying between the leaves of the mesentery of the jejunum and partly fused with the jejunum. This pouch had two orifices, one near each end, which communicated with the intestine. There was a perforating peptic ulcer near the proximal orifice but no mention is made of gastric mucosa being found in the diverticulum. There was also a large retromediastinal enterogenous cyst attached to the thoracic vertebrae. The child had tarry stools for ten days before death.

A giant diverticulum in a five-year-old girl was reported from the Mayo Clinic, first by Dixon and Famiglietti,[15] in 1937, and later by Goldstein and Cragg,[16] in 1938. This diverticulum was 61 cm. long; it contained gastric mucosa and a typical peptic ulcer. The diverticulum and ileum were described as having a common mesentery. The diverticulum joined the ileum at the mesenteric border, and its distal end was buried in the mesentery. The child had tarry stools from the age of six months, and abdominal pain from the age of two years. Operation resulted fatally.

Harild,[17] in 1937, reported a three-year-old boy who died from peritonitis following perforation of an ulcer of the ileum. The ulcer was situated 1 Mm. from the opening of an intramesenteric diverticulum, 50 cm. long, which was lined with gastric mucosa. This child also had bloody and tarry stools after the age of seven months.

Normark,[3] from Upsala, Sweden, in 1938, described a successful operative case of an intramesenteric diverticulum in a two-year-old boy who had tarry stools after the age of two and one-half months. There had also been occasional nausea and vomiting, and once severe abdominal pain. At operation, an intramesenteric small bowel diverticulum, 15 cm. long, was found, which was lined with gastric mucosa. In the ileum, near the mouth of the diverticulum, was a typical peptic ulcer. Resection of diverticulum and adjoining ileum was performed, with recovery.

SUMMARY AND CONCLUSIONS

Report is made of a child successfully operated upon twice for closure of perforations in the small intestine, and a third time for resection of 42 cm. of ileum, together with an intramesenteric giant diverticulum (duplication) 27 cm. long. The diverticulum was lined with gastric mucosa, and the perforations occurred in typical peptic ulcers adjoining one of the two openings between the diverticulum and the intestine.

The unusual clinical features of the case are discussed with special reference to diagnosis, difficulties encountered in recognizing intramesenteric diverticula at operation, and technical problems in removal of such diverticula.

The findings in this case indicate that such anomalies are not true Meckel's diverticula, but probably develop from the intestinal epithelial nodules found by Lewis and Thyng in early animal and human embryos. The writer's study of serial sections of a 6 Mm. human embryo showed three such primitive diverticula.

The use of the term "duplications of the alimentary tract," in referring to the entire group of enterogenous cysts and diverticula, obviously not of Meckelian origin, is advocated.

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TOPOGRAPHY AND DEVELOPMENT OF THE CECUM-APPENDIX

CHARLES F. DE GARIS, M.D., PH.D.

OKLAHOMA CITY, OKLA.

FROM THE DEPARTMENT OF ANATOMY, UNIVERSITY OF OKLAHOMA SCHOOL OF MEDICINE, OKLAHOMA CITY, OKLA.

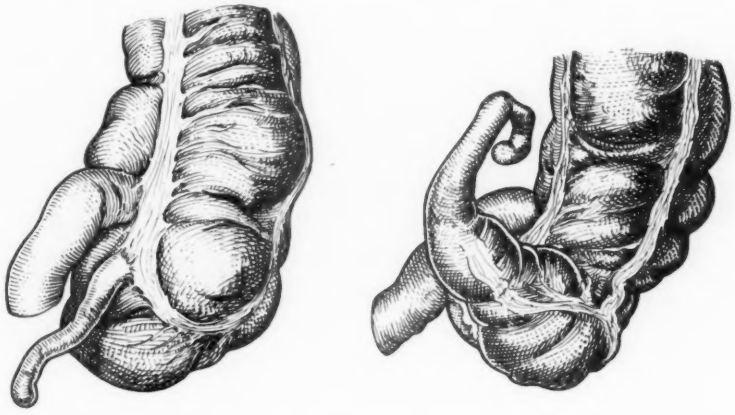
THE APPENDIX is said to be the only organ in the body which has no normal position (Maingot[1]). A valid objection to this statement concerns the restrictive word *only*. Other abdominal viscera such as the stomach, jejuno-ileum, transverse colon and sigmoid are variously more mobile than the appendix, and in the living subject, as seen by roentgenographic silhouettes of induced opacities, these organs are very diverse in position, not only from one individual to another but also in the same individual at different times under different degrees of filling and under other changing physiologic conditions. However, Maingot's statement is of value in emphasizing the fact that the appendix is frequently one of the mobile viscera, even though its lack of normal position is not in itself remarkable.

Contours of the Cecum.—Where the appendix is at any given time depends largely on the cecum; and the cecum in turn is subject to wide fluctuations of contour and to some change of position as a result of tonus, peristaltic activity and contents. The contours of filled and empty ceca and the effect of these states on the appendix are well shown in Figs. 1 A and B. These represent the usual or so-called normal ceca viewed from behind, this view showing better than any other the convergence of the three taeniae coli at the root of the appendix. It is seen that with the cecum distended (Fig. 1 A) the appendix has a dependent position, while with the cecum contracted (Fig. 1 B) the appendix is turned sharply upward in a retrocecal position.

It may be objected that the two specimens placed in juxtaposition (Fig. 1) are simply two different types of ceca, or at any rate ceca taken from two different cadavers. This latter objection is of course valid as far as cadaver anatomy goes. These are, indeed, two different specimens, with the peritoneum removed in each case to show more clearly the course and termination of the taeniae coli. Yet from a comparison of these specimens certain deductions may be made regarding the effects of contraction on the cecum and appendix. In Fig. 1 B it is seen that the apparent root of the appendix is much enlarged, as if cecal contents had been forced into it. But this is not at all the case, for the reason that the apparent root of the appendix is, in fact, the appendicular zone of the cecum itself with its musculature strongly contracted; one of the taeniae is clearly visible over this bulbar enlargement. The musculature of the appendix is also contracted; the longitudinal muscle, as a continuous tunic formed by convergence of the taeniae, has shortened and kinked the appendix.

Submitted for publication August 29, 1939.

Peristalsis and the Ileocecal Valve.—The foregoing comparison of distended and contracted ceca calls for a brief consideration of the movements of the large intestine, especially as they affect the ascending colon and cecum. Cannon,[2] studying movements of the large intestine in the cat roentgenologically, found that in the distal transverse and descending colons the contents



A B

FIG. 1.—The cecum-appendix viewed from behind. (A) Cecum distended and appendix directed downward. (B) Cecum contracted and appendix turned upward. In both specimens the peritoneum has been removed to demonstrate more clearly the taeniae coli. (Redrawn from Spalteholz.)

are moved toward the rectum by peristaltic waves, but in the ascending and proximal transverse colons the more frequent movement is antiperistaltic. The contents in these parts are liquid and set up running waves of contraction toward the ileocecal valve, such waves being separated by long periods of rest. Cannon's assumption is that the ileocecal valve prevents return of cecal contents to the ileum.

Hurst[3] and others, from roentgenologic examinations in men, find a different type of movement which they call "mass peristalsis," *i.e.*, strong but brief movements of contents from one part of the large bowel to the next, such movements being connected with the act of eating by an alleged gastrocolic reflex set up by entrance of food into the stomach. Contents are said to traverse the colon at long intervals by sudden displacements due to the "mass peristalsis." In latent periods the only activity is that of "haustral churning," whereby the contents are subject to local, nonprogressive agitation from contraction of the haustra.

While roentgenographic methods are the only ones affording a direct visual study of normal intestinal movements, it is obviously difficult to employ such methods on the large intestine where rest periods are so lengthy. In this connection, one traditional view must be corrected with emphasis: The ileocecal valve is not, in a strict functional sense, a valve to prevent return of cecal contents into the ileum, nor is such return prevented by the so-called ileocecal sphincter. This assertion is based upon the repeated experience of clinical roentgenologists, who find that when the entire large intestine is filled

with a barium enema a variable length of terminal ileum usually appears in the roentgenogram.

Effects of Growth and Gravity on the Cecum-Appendix.—Another factor seldom fully considered in the literature is that of gravity as it operates on the several parts of the large intestine. With an individual in the prone position, all movements of contents of the large intestine may be regarded as merely translational in, or upon, the same plane, this being an approximately horizontal one. But when the individual stands erect, the segments of the large intestine are at once resolved into two diametric opposites with respect to gravity. The cecum, ascending colon and distal limb of the transverse colon have to propel their contents against a gravitational field, while the proximal limb of the transverse colon and the descending colon have exactly the opposite task. In brief, the dynamics of one group of segments is to lift weight, that of the other group is to lower it.

This difference in dynamics is clearly reflected in the state of filling of the two groups of segments. Thus, the descending colon, where in the upright posture weight is lowered, usually presents itself as a contracted, empty tube. On the other hand, the distal limb of the transverse colon, where weight must be raised from the most dependent part of the loop through a steep ascent to the splenic flexure, is, in any posture, usually filled with gas and semisolid contents. The proximal limb of the transverse colon, a weight-lowering segment, may or may not be filled, depending on the quantity of contents of the whole loop. Finally, the ascending colon and its cul-de-sac, the cecum, are, in most positions, filled to distention, since their work is to raise a column of liquid contents against gravity until such contents pass the brim of the ascending colon at the hepatic flexure.

With the foregoing facts in mind, there is a tendency to view the cecal cul-de-sac as merely a distention due to the column of contents which it supports. However, this view does not take into account the known embryology and comparative anatomy of the cecum, for example as presented by Huntington,[4] Kelly and Hurdon,[5] and Keith.[6] The cecum and appendix are structures in their own right, *i.e.*, their ontogeny is quite distinct and independent of any weight-bearing function. Even so, a suggestive relation between weight-bearing and cecal contour will be discussed below.

Interesting as it would be to consider the comparative anatomy and embryology of the cecum-appendix, attention must be confined to the classic human types (Fig. 2). In type A, the infantile contour, the cecum is a pyramid with the appendix arising from the inverted apex. In type B, found most frequently in early years of childhood, there is a symmetrical growth-distention of right and left sides, with the appendix attached to the most dependent part of the cecum. Type C exemplifies the usual adult form of the cecum, where there has been a differential growth-distention in favor of the right ventral aspect of the cecum, in such degree as to cause the appendix to arise distinctly to the left and dorsally, one to one and one-half inches (2.5 to 3.7 cm.) below the ileocecal valve. Normal variations in cecal contour may be said

to have their distribution on either side of type C, with diversities arising from the degree of growth-distention of the right side, to which latter circumstance is largely due the relative distance of the appendix from the ileocecal valve. With excessive extension of the right wall of the cecum the root of the appendix may lie close to, or even somewhat behind, the ileocecal junction.

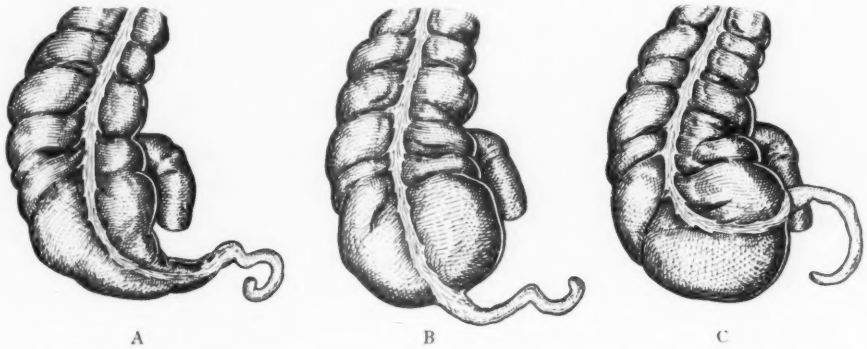


FIG. 2.—(A) The infantile cecum-appendix. (B) The cecum-appendix during early years of childhood. (C) The usual adult cecum-appendix, where the appendix arises dorsally and to the left as a result of growth-distention of the right ventral wall of the cecum. All three specimens are viewed from in front.

The three types, A, B and C, offer a suggestive sequence of development in the light of the aforesaid weight-bearing properties of the cecum. Type A, the infantile or nonweight-bearing cecum, is in fact strikingly similar to the adult contracted cecum of Fig. 1 B. During the early years of childhood the first contour of the weight-bearing cecum (Fig. 2, type B) is a fairly symmetrical growth-distention of right and left sides. The adult cecum (type C), representing a long period of weight-bearing, shows a variable, but usually high, degree of growth-distention on the right side.

The term "growth-distention," used in the above discussion, may seem to beg the question. Yet a summary of the evidence and reasoning on this point will indicate the propriety of this term. The cecum and appendix are, as already mentioned, developmental structures in their own right, wholly independent, as far as ontogeny is concerned, of any function of weight-bearing. From a consideration of the digestive tract as a whole, the cecum appears as a midgut expression of that general tendency toward diverticulum formation, which in the foregut gives rise to such important structures as the liver and pancreas. The hypothesis offered here to account for the contour of the cecum is as follows: Given in the newborn a diverticulum, the type A cecum-appendix, with this taking a position in the right iliac fossa at the lower end of the ascending colon, when the child assumes more and more the upright posture, the weight-bearing function becomes increasingly a factor in shaping the contour of the cecum. Also during these early years of childhood the cecum shares in the linear and lateral growth of the gastro-intestinal tract, while the lymphoid tissue of the appendix grows more rapidly than other parts of this organ, which latter as a whole continues as a vestigial structure with progressive reduction of lumen. Accordingly, the type B cecum-

appendix may be regarded as a resultant of weight-bearing and intrinsic growth, the conspicuous manifestation of which is a fairly symmetrical growth-distention of right and left sides of the cecum.

As weight-bearing and growth continue with increasing age of the individual, a differential is set up in favor of the right wall of the cecum, this by reason of the ileocecal junction and by the blood supply of the appendix, both forming a drag or fixation for the left wall. This differential appears to operate largely as the result of weight-bearing, and once set up is readily extended to produce the definitive type C of the adult cecum-appendix. Thus, it is held that the changes of cecal contour from A through B to C are the net results of growth and gravity, or as expressed above, growth-distention. Even where gravity appears to account for the enlargement of the right wall of the cecum, as in the transition from B to C, there is still the possibility that weight-bearing may in itself be something of a growth-promoting agent.

The foregoing hypothesis is well supported by contours of the cecum-appendix in anomalous positions. Thus in cases of undescended cecum the contour is either that of type A or type B (Fig. 2); in other words the usual right-sided growth-distention (producing type C) has not occurred because in these cases the weight-bearing of cecal contents is not a factor in shaping the cecum. On the other hand, where the cecum has descended and in so doing has become inverted, there are varying degrees of right-sided growth-distention, depending both on the length of the inverted segment and on the amount of traction exerted by the ileum and the blood vessels of the cecum-appendix.

Positions of the Appendix.—In view of the fact that the appendix is frequently mobile, it seems that undue attention has been given to its supposed directions. This is not to minimize the importance of two general categories of appendix: (1) The adherent retropostures (behind the colon, cecum or ileum); and (2) the freely mobile, which latter may be postcecal or otherwise directed. The developmental sequence by which one or other of these appendices is produced should here be mentioned briefly.

It will be recalled that at the tenth week of fetal life the midgut loop returns by normally definite sequence through the umbilical orifice to the abdominal cavity (Dott[7]). On completion of this return the cecum first lies free near the umbilicus and ventral to the small intestine and mesenteric artery. However, the colon now begins to straighten and carries the cecum with it upward and to the right, the colon itself lying across the pedicle of the intestinal mass and mesenteric artery, the cecum lodging beneath the liver. Subsequently, by apparent retraction of the liver and by linear growth of the colon, the cecum reaches its final position in the right iliac region. This descent of the colon from liver to iliac region may, and often is, attended in transit by a folding under of the appendix, which latter forms an inclusion behind the colon during peritoneal fixation of this part of the large bowel. On the other hand, if the appendix remains free and directed caudally during the whole descent of the cecum, then, after fixation of the colon, it is left as

a permanent and definitive organ of great mobility, barring of course subsequent pathologic episodes which may render it adherent.

The fixed and mobile categories of appendix are not especially emphasized by Wakeley[8] in his study of 10,000 cadavers. He merely classifies the appendix according to its various directions thus: Retrocolic or postcecal 65 per cent; pelvic 31 per cent; postileal, preileal and subcecal 4 per cent. To most surgeons and anatomists the very high incidence given by Wakeley for retropostures of the appendix will doubtless seem far out of line with their own experience. His incidence of 65 per cent includes all appendices retroposed to cecum and colon, whether adherent or lying free in the retrocecal fossa. To be sure, his series of 10,000 cadavers is much larger than any other known to us at present. Even so, the trend of smaller series is uniformly toward preponderance of the three to six o'clock quadrant of directions rather than toward what may be interpreted as the 9 to 12 o'clock quadrant of Wakeley's series. Thus Kelly and Hurdon give the following directions of the appendix, listed in order of frequency—(1) into pelvis; (2) along iliac vessels; (3) to promontory of sacrum; (4) behind cecum; (5) under ileum; (6) lateral to cecum; (7) into iliac fossa; (8) among coils of small intestines; and (9) mesial to cecum over ileum. The above listing is evidently drawn more or less from data of other reports, concerning which Kelly and Hurdon remark: "The literature on the subject of positions of the appendix is full of the most elaborate statistics, but as they make unprofitable and difficult reading, they have been largely omitted and only the average of the combined results is given." It seems to us, too, that elaborate statistics on this question are unprofitable, not so much as a matter of difficult reading, but because, in so far as they deal with the mobile appendix, they probably have no real significance.

Historical Résumé.—The history of the diseased appendix, like that of circulation of the blood, is an extended chronicle of misinformation, misjudgment and obscurant terminology. Abscesses in the right iliac fossa had long been recognized as frequent and peculiarly fatal. But the only organ in this region capable of producing such disturbance was thought to be the cecum. So, through many decades of dismal controversy, there arose such terms as typhilitis, perityphilitis, paratyphilitis, typhlo-enteritis, and what not, all focusing attention on the cecum as the sole offending part. This being a period when the surgeon-anatomists were making headlong advances in other fields, it must seem to us now tragically odd that autopsy findings of that time were so grossly misinterpreted.

The appendix was, of course, known, but only as an insignificant rudimentary structure, to which no one thought of attributing any special pathology. The prevailing syllogism of that day appears to have been: (1) Only a large organ in the right iliac fossa can produce a large abscess (or grave prognosis). (2) The cecum is the only large organ in the right iliac fossa. (3) Therefore, the cecum produces the large abscess (or grave prognosis). This tacit correlation between the size of the organ and the size of the

abscess or gravity of prognosis did eventually, and reluctantly, give way to a clear recognition of the appendix as the organ involved, the idea finally being crystallized in explicit terminology. The first use in all literature of the word *appendicitis* appears in the following sentence from the classic paper by an American, Reginald Fitz,[9] in 1886: "As a circumscribed peritonitis is simply one event, although usually the most important, in the history of inflammation of the appendix, it seems preferable to use the term appendicitis to express the primary condition." If Fitz did nothing more than give the correct name to a specific pathology, his communication would have been notable; but as a matter of fact his review of the history, his understanding of the condition itself, his statistical treatment and his recommendation of early surgical intervention were, indeed, the stroke of a master.

Another contribution soon to appear was that of Charles McBurney,[10] in 1889, who defined the well-known point bearing his name as follows: ". . . I refer again to the important aid to diagnosis of which I have already spoken, namely, the ascertaining, by the pressure of a single fingertip, that the point of greatest tenderness is, in the average adult, almost exactly two inches from the anterior iliac spine, on a line drawn from this process through the umbilicus. Much greater tenderness at this point than at others, taken in connection with the history of the case and the other well-known signs, I look upon as almost pathognomonic of appendicitis. This point indicates the situation of the base of the appendix, where it arises from the cecum, but does not by any means demonstrate, as one might conclude, that the chief point of disease is there. The abscess, or concretion, or cyst may be at quite a little distance, but the greatest pain, on pressure of one finger, will be felt at the point described."

The diagnostic value of a single point of greatest tenderness in appendicitis is too familiar to require comment. But there were weaknesses in McBurney's pathologic anatomy. In the first place, he defines precisely a surface point, which actually may have a wide range of variation, depending on sex, constitutional type and state of nutrition of the individual. In the second place, he undertakes to make this surface point coincide with a very definite point of underlying visceral topography, namely the junction of appendix and cecum. It is now thoroughly recognized from roentgenologic studies that the topographic point of junction of appendix and cecum is extremely variable. Barclay[11] has an interesting demonstration (his Fig. 86) of a skeletal outline, whereon the sites of the cecal end of the appendix are traced from 30 unselected roentgenograms. In not a single case does this site coincide with McBurney's point; in only seven does it fall within a small circle around the point; in ten it is above the spino-umbilical line, far medial to the point; in 13 it is below the spino-umbilical line, seven of these being medial to the point, six lateral to it. Thus, in only seven out of 30 cases does the junction of appendix and cecum fall any way near McBurney's point. The distribution of these sites in the Barclay illustration prove, as

well as anything could, the futility of a rigid, preroentgenologic concept of surface topography, as applied to the mobile viscera.

Again, as for McBurney's point, the confusion arising from variability is further confounded by compilers of anatomic text-books setting up definitions of their own invention, though still, for some reason, retaining the name McBurney to identify the point defined. Where students, such as ours, use a number of different texts, and find among them at least three diverse specifications for McBurney's point, one can well assert that the resulting confusion is complete. If eponyms must be used—and there seems no present way of eradicating them—then, in plain deference to historic accuracy, they should be used in their original meaning. While the name McBurney, associated with a single point of greatest tenderness in appendicitis, is doubtless of value in emphasizing the existence of such a point, whose diagnostic worth no one disputes, it is our contention here that to give precise topographic definition to such a point is beyond the possibilities of sound human anatomy.

SUMMARY

The appendix is frequently one of the mobile viscera of the abdomen. Its position at any given time depends largely on the cecum, which latter varies in contour and even in position, as a result not only of type but also of peristaltic activity, state of filling and other physiologic conditions. Three general types of ceca, (1) the infantile; (2) that prevailing in early childhood; and (3) the adult, may be regarded as a developmental sequence. The factors of intrinsic growth and of gravity (weight-bearing of cecal contents) are considered in the evolution of the cecum from infantile to adult types. The directions taken by the appendix are not regarded as significant, when the appendix itself is mobile. From this it follows that but two general categories of appendix are proposed, the fixed and the mobile. Two historic events are recounted in connection with the diseased appendix, *viz.*, the first use of the word appendicitis, proposed by Fitz, in 1886; the designation of the point of greatest tenderness in appendicitis by McBurney, in 1889. The futility of defining McBurney's point is recognized, especially in reference to the highly variable topography of the junction between appendix and cecum.

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BENIGN TUMORS OF THE OVARY ASSOCIATED WITH ASCITES AND PLEURAL EFFUSION*

REPORT OF A CASE OF MULTILOCULAR CYSTADENOMA

WILLIAM F. MACFEE, M.D.

NEW YORK, N. Y.

WITHIN recent years an increasing number of benign tumors of the ovary associated with ascites and pleural effusion have been reported. The tumor in each instance has been an unilateral or bilateral fibroma.

It is obvious that the total number of such cases cannot be very large because fibroma itself as Peterson[1] and Kelly[2] have observed, is one of the rare ovarian tumors. Nevertheless a considerable number of fibromata have been recorded. Doran[3] reported 11 cases in 1896, Dartigues,[4] in 1899, included 20 cases of fibroma in a monograph on solid tumors of the ovary, and Peterson,[1] in 1902, described two cases of his own, to which he added 82 cases from the literature. In 1923, Hoon[5] reported 55 cases from the Mayo Clinic.

An associated ascites has been a frequent but not a constant finding. It was present in five, or 45 per cent, of the 11 cases reported by Doran[3]; in 34, or 40 per cent, of the 84 cases reviewed by Peterson[1]; and in 14, or 25 per cent, of the 55 cases reported by Hoon.[5]

Pleural effusion as well as ascites is sometimes found but much less frequently than ascites alone. In 1879, Cullingworth,[6] of Manchester, described what appears to have been an authentic case. The patient, a widow, age 36, was admitted to St. Mary's Hospital, Manchester, England, March 11, 1879, because of slight uterine hemorrhages of three months' duration. At that time, she was described as having a florid complexion and as being apparently in good health. The hemorrhages ceased about the middle of June, 1879, from which time the patient's health rapidly declined. She lost flesh and ascites supervened. She suffered also from pleurisy, first on the left side, where an effusion took place, and subsequently on the right side, where loud friction sounds were audible to within a short time of her death. On September 10, 1879, she became suddenly worse, with symptoms of intense dyspnea and general collapse, and died the following day.

At autopsy, the left pleural cavity was found full of fluid, and the whole of the left lung was entirely collapsed. On the right side, the lower lobe was firmly attached by recently formed adhesions to the diaphragm and chest wall, and the whole lung was congested and edematous. There was a large quantity of fluid in the peritoneal cavity and the peritoneum was thickened and opaque. Large, bilateral, solid tumors of the ovaries were found. After microscopic examination, Doctor Dreschfeld, of Owens College, made a diagnosis of ovarian fibromata.

* Read before the Pan-Pacific Surgical Association, Honolulu, T. H., September 20, 1939. Submitted for publication November 20, 1939.

In the discussion which followed Mr. Cullingworth's presentation, Mr. Lawson Tait observed that the ascites and pleural effusion seemed to him to be of very great importance in both the clinical and pathologic aspects of the case. He stated that he had observed a number of cases of ovarian tumors complicated with cancer, and in several the rapid effusion of pleural fluid had been the cause of death. Because of this fact he was not disposed to accept Mr. Cullingworth's specimen as necessarily one of a nonmalignant character. Doctor Wiltshire also thought that the pleural effusion was strongly suggestive of malignancy, unless there was some other cause for it, for example, acute pleurisy.

In reply, Mr. Cullingworth said that the possibility of cancerous origin of the effusion into the pleural and peritoneal cavities had been considered at the autopsy, but that very careful and minute inspection failed to discover more than a thickened and opaque condition of the pleura and peritoneum.

For a further report, the specimen was referred to a subcommittee, consisting of Mr. Alban Doran and Mr. Knowsley Thornton who thought the term mixed sarcoma would most correctly describe both tumors. In presenting their report, however, they stated that the tumors, owing to postmortem changes and to the action of alcohol, were not in a satisfactory condition for accurate examination of their more delicate cell structures.

In spite of the report of this subcommittee, one is impressed by Mr. Cullingworth's observations, and in the light of our present knowledge it appears probable that this case was one of benign ovarian fibromata associated with peritoneal and pleural effusion. It is also likely that this is one of the first, if not the first, to appear in the modern literature.

Pleural effusion was observed in one of the cases reported by Doran,[3] and Dartigues[4] listed it among the complications of ovarian fibroma. Owen,[7] in 1923, stated that it might occur, but he was not able to detect it in the case he reported. Two of the 55 cases reported by Hoon[5] had bilateral hydrothorax as well as ascites. A single case of ovarian tumor with ascites and pleural effusion was reported in detail by Leo[8] in 1926. His description, however, does not reveal the identity of the tumor. Salmon,[9] in 1934, described two cases of ascites and pleural effusion coexisting, in one case with an ovarian fibroma, and in the other with a fibroid tumor of the uterus. In his book on "Tumors of the Female Pelvic Organs," published in 1934, Meigs[10] described three such cases from the Massachusetts General Hospital, and, in 1937, he and Cass[11] reported these with an additional case from the Massachusetts General, and three cases from the literature, making a total of seven cases. They called attention to the possible existence of hydrothorax as well as ascites in cases of benign fibroma and emphasized the importance of recognizing this possible association.

In discussing the presentation of Meigs and Cass,[11] Dr. W. T. Dannreuther, of New York, reported the removal of a tumor which had the gross appearance of an adenocarcinoma but which proved to be benign and which was associated with fluid in the abdomen and right chest. According to

more recent information[12] this patient remained well for two years and then again developed ascites which progressed rapidly. Abdominal exploration revealed inoperable carcinoma from which the patient died within a month. During her last illness, however, there was no evidence of a pleural effusion. Continuing the discussion of the work of Meigs and Cass,[11] Dr. T. E. Jones,[17] of Cleveland, and Dr. W. T. Black,[16] of Memphis, each reported a case of ovarian fibroma with ascites and hydrothorax. Jones's case had been previously operated upon for carcinoma of the breast and was thought to have abdominal metastasis. She was cured by aspiration of the chest fluid and removal of the ovarian tumor. The true condition in Black's[16] case was discovered at autopsy. Rhoads and Terrell[13] described a single case in 1937, and, in 1938, Weld[14] reported two cases. In his last article on the subject Meigs[15] reviewed a total of 15 cases, including the original seven.

The case which is herewith reported in connection with the present discussion—a multilocular cystadenoma—appears to constitute an exception to the type of ovarian tumor which has ordinarily been associated with ascites and pleural effusion.

Case Report.—Hosp. No. A6439: E. B., white, female, age 54, was admitted to St. Luke's Hospital, November 23, 1938. Her chief complaints were swelling of the abdomen, shortness of breath, loss of appetite, weight, and strength.

For about one year the patient had observed a steady increase in the size of her abdomen. It had gradually become so large and heavy that she could no longer pursue her usual activities. At the same time there was a loss of flesh from other parts of her body. During the few weeks preceding her admission to the hospital she became very dyspneic and experienced, almost constantly, a distressing sense of suffocation. It had been necessary for her to remain in bed most of the time with the head and thorax elevated. There had been no pain in the abdomen or chest and only a slight dry cough, but her nights were disturbed by profuse sweating.

The past history was irrelevant. There had been two abortions, each at three months, and no children. The menopause had occurred three years previously without untoward incident. One year before admission there had been some vaginal bleeding which persisted three weeks and then subsided spontaneously.

Physical Examination.—The patient was generally emaciated. Excursions of the right chest were limited and the physical signs indicated the presence of fluid over almost the whole of the right lung field. The abdomen showed great enlargement, and exhibited a fluid wave and the usual signs of ascites. A large tumor could be felt extending from below the level of the pubis to the upper abdomen where it disappeared under the costal margins. A slight irregularity of its surface could be felt in the left subcostal region. On pelvic examination, the cervix was found to be displaced anteriorly by a tense mass which projected downward behind the uterus.

A roentgenogram (Fig. 1) showed density throughout the right chest suggesting a right pleuritic effusion. The blood count was: R.B.C. 4,850,000, hemoglobin 96, W.B.C. 10,200, polymorphonuclear leukocytes 87, lymphocytes 9, large mononuclear and transitional cells 4.

The right chest was aspirated, and 1,500 cc. of dark, yellowish-green fluid were removed. The fluid contained desquamated pleural cells and a few lymphocytes. No tumor cells were found in the centrifuged specimen, and no tubercle bacilli could be demonstrated. A guinea-pig, inoculated with the fluid, showed no sign of tuberculosis after six weeks.

In view of the markedly distended abdomen, the pleural effusion, the loss of appetite,

weight, and strength, a tentative diagnosis of ovarian carcinoma with peritoneal and pleural metastasis was made. Operation was decided upon in the hope that removal of the large tumor might alleviate the condition to some extent and enable the patient to enjoy, for a time at least, a greater degree of activity.

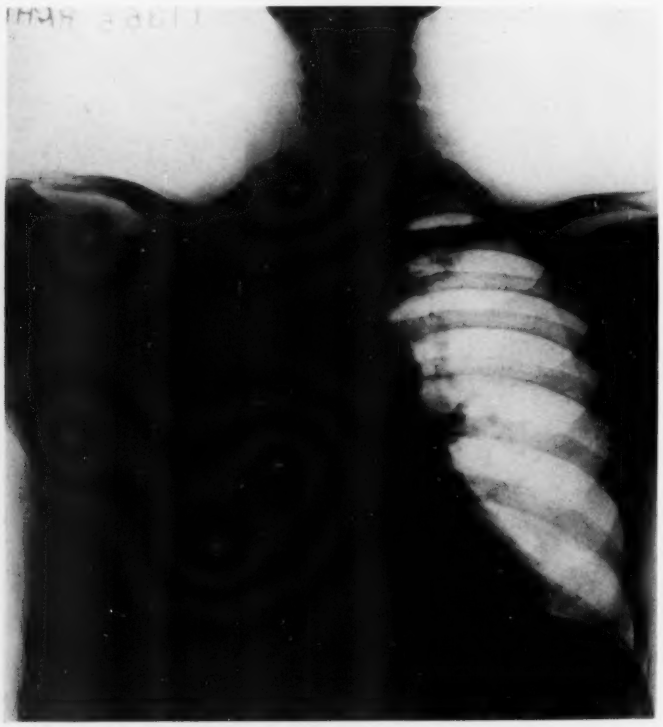

FIG. 1.—Roentgenogram of the chest upon admission showing right chest filled with fluid.

Operation.—December 1, 1938: A tumor which filled the entire abdomen was removed (Fig. 2). It arose from the left ovary and was attached by a rather thin pedicle. There was a relatively small amount of free, amber-colored fluid in the abdomen, but no peritoneal implants or other definite evidence of malignancy. The right ovary appeared to be essentially normal, but it was removed because the process in the left ovary was considered to be probably malignant.

Pathologic Examination.—Gross: "The specimen consists of a large left ovarian cyst and tube. The cyst measures 27 x 30 x 14 cm. and weighs 17 lbs. It is covered with a smooth, tough, membranous gray wall. There are several irregularities of the surface. The left tube measures 11 cm. long and 0.7 cm. in diameter and is attached to the cyst. It appears normal. On section, the cyst is made up of many smaller cysts containing fluid of varying consistency; some are filled with material of sebaceous character, some with thick greenish fluid, and some with clear thin fluid. There are numerous cellular nodules throughout.

"The right ovary and tube, closely bound together by adhesions, are also present. The tube is sealed but only slightly distended. The serosa is rough.

"The piece of omentum measures 12 x 6 x 0.5 cm. and is slightly roughened, but shows mostly orange fat in a thin web of peritoneum and no gross tumor. The ovary is small and shows one small cystic follicle."

"*Microscopic.*—Sections through the wall of the left ovarian cyst show that there is a dense fibrous capsule within which there are masses of adenomatous tissue, with the formation of some discrete glands and without much mucous content. In others, there is hypersecretion but the cells are not of the tall columnar type such as is found in multilocular pseudomucinous cysts. The tumor is apparently a less differentiated one, although closely related. All of the cells appear to be limited by the basement membrane, and there is no evidence of invasion through the wall or of a primary malignant process (Figs. 3 and 4)."

The right ovary contains a small epithelial-lined cyst which may have the same origin as the large one. There are also calcified areas throughout the ovary; these also, in some instances, being lined with a layer of columnar cells. These cysts have probably both arisen from congenital remnants which are numerous in both ovaries, but the process appears to be benign in each. The tube shows some dilatation and chronic inflammation. *Pathologic Diagnosis:* Multilocular cystadenoma of left ovary. Epithelial ovarian cysts, right ovary. Chronic salpingitis.

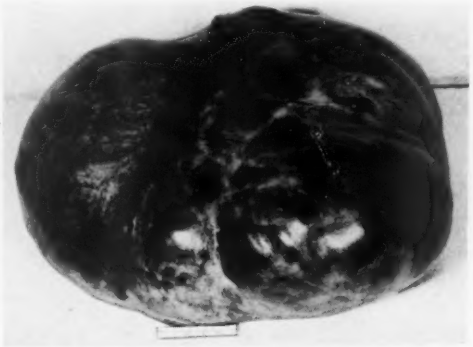

FIG. 2.—Photograph of the cystadenoma removed at operation. Weight 17 pounds (approximately 8 Kg.). Scale in centimeters.

Subsequent Course.—On the tenth postoperative day 1,500 cc. of additional fluid were removed from the right chest; a roentgenogram taken after the removal showed

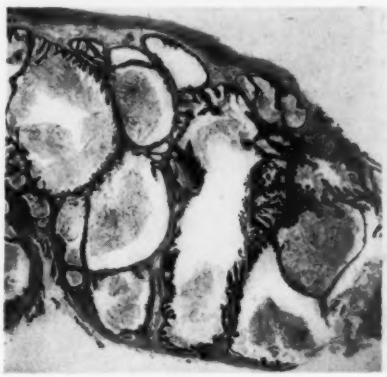

FIG. 3.—Photomicrograph showing multilocular character of tumor. (Low power)

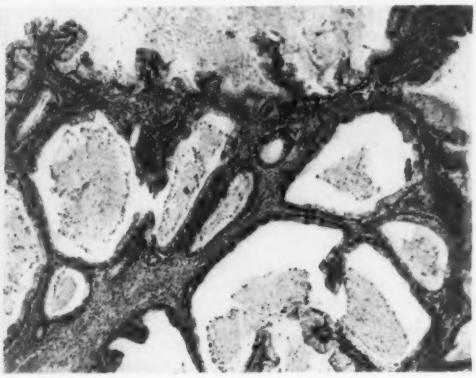

FIG. 4.—Photomicrograph showing the limitation of the lining epithelial cells by basement membrane and the benign character of the histologic structure. (High power)

no evidence of tuberculosis or other pulmonary disease (Fig. 5). There was no further accumulation of fluid, and convalescence was uncomplicated with the exception of the night sweats which persisted for about three weeks and then ceased. The patient gradually regained her appetite, weight, and strength, and was entirely well when last heard from, November 2, 1939, 11 months after operation.

In the case herewith reported the tumor was a multilocular cystadenoma, but, in all other essential respects, it was similar to the cases of fibroma which have been previously reported, and fits into the symptom complex described

by Meigs and Cass.[11] The predominating symptoms were related to interference with proper aeration, and the physical findings were similar to those observed in cases of ovarian fibroma with ascites and pleural effusion. Ablation of the tumor and removal of the pleural fluid likewise terminated the disease.

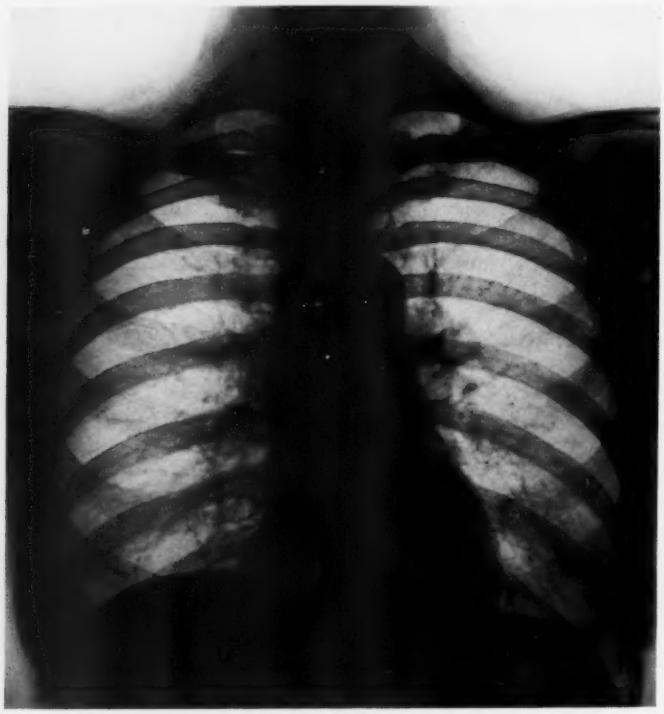

FIG. 5.—Roentgenogram at the time of the patient's discharge from hospital, 23 days after operation, showing chest clear.

The amount of fluid in the chest and the rapidity of its reaccumulation has varied considerably, and no satisfactory explanation of its occurrence has been offered. In the case described by Rhoads and Terrell[13] the effusion was massive and thoracenteses were performed five times within a month; fluid in amounts ranging from 1,000 to 3,000 cc. was removed each time. Leo's[8] patient also required the removal of large amounts of pleural fluid at frequent intervals. In the case just described there were two aspirations of the chest, one a week before operation and the other ten days postoperative. An associated ascites has been found in all the cases which have had pleural effusion, and cachexia has been frequent. Removal of the ovarian tumor and aspiration of the chest fluid has been sufficient to effect a cure in all patients who have been operated upon. Three patients, one reported by Cullingworth,[6] one by Doran,[3] and one by Black,[16] died without operation, the true condition being discovered at autopsy.

CONCLUSIONS

It appears sufficient to call attention, as Meigs and Cass[11] have done: First, to the possible coexistence of ascites and pleural effusion in association with a benign tumor of the ovary; and second, to the possibility of effecting a cure by simple removal of the tumor.

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STUDIES ON THE CEREBROSPINAL FLUID PRESSURE IN UNANESTHETIZED DOGS

JOHN E. WEBSTER, M.D.,

AND

NORMAN E. FREEMAN, M.D.

PHILADELPHIA, PA.

FROM THE HARRISON DEPARTMENT OF SURGICAL RESEARCH, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

I. PHYSIOLOGIC RESPONSES TO THE ADMINISTRATION OF INTRAVENOUS FLUIDS IN NORMAL ANIMALS

THE PRACTICE of dehydrating patients with cerebral trauma indicates that there are those[9] who believe that even a normal fluid intake is harmful under these circumstances. The administration of isotonic fluids is supposed to increase the cerebospinal fluid pressure.[9] Clinical observations which we[12] reported previously, however, demonstrated that large quantities of isotonic fluids could be administered to patients with cerebral trauma without significantly increasing the cerebrospinal fluid pressure. The present experiments were undertaken upon normal dogs preliminary to experiments upon dogs with cranial injuries, in order to obtain further information on the effect of isotonic and hypertonic solutions upon the cerebrospinal fluid pressure. Since the observations on patients with cerebral trauma were performed under local anesthesia, similar conditions were used in the experiments reported in this paper.

Method and Procedure.—Mongrel female dogs, weighing approximately 10 Kg., were used in these studies. The animals were fed a mixed diet and given 500 cc. of milk 12 hours before beginning the experiment. After a three-inch bandage was bound over the untrained dog's eyes, the animal remained immobile for hours as it lay on its right side. The willingness to remain quiet and to tolerate the intravenous injection, and maintenance of a needle in the cisterna magna we attributed to the blindfolding. The animal was catheterized. Under local anesthesia, with aseptic precautions, a No. 22-gauge lumbar puncture needle, one and one-quarter inches long, was inserted into the cisterna magna. To the needle, a short segment of rubber tubing and a one Mm. bore manometer were attached. Six-tenths cc. of fluid was required to fill the system to the 50 Mm. mark on the manometer. Throughout the experimental period, the pressure was recorded every ten minutes, and during the injection period five-minute readings were made. An irregular rise or fall in pressure was not recorded unless the change persisted for more than one minute.

In the first group of control experiments, physiologic saline solution was

Submitted for publication August 16, 1940.

used in the manometers. The solution was prepared from compressed tablets of sodium chloride dissolved in single-distilled water. Cell counts were made upon specimens of the cerebrospinal fluid taken at the beginning and end of each experiment, using the technic of Merritt and Fremont-Smith.[19] A gradual rise in the cerebrospinal fluid pressure with pleocytosis was observed in most instances. When a marked pleocytosis was observed, there was a gradual rise in the cerebrospinal fluid pressure in every instance.

Influence of Fluid Used in Manometer Upon Cerebrospinal Fluid Pressure and Pleocytosis.

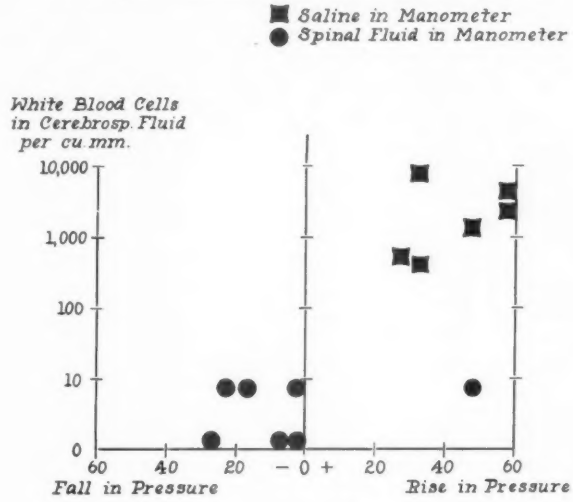

Chart 1.

When the experiment was repeated with the needle alone in the cisterna magna, pleocytosis was not observed. When 0.6 cc. of spinal fluid was used in the manometer in place of the saline solution, the rise in cerebrospinal fluid pressure and pleocytosis were no longer encountered, except in the one instance where a rise in pressure occurred without pleocytosis. Chart 1 illustrates the influence of the fluid used in the manometer upon the cerebrospinal fluid pressure and the presence of white blood cells in this fluid.

In the later experiments, cerebrospinal fluid either from the experimental animal or from another dog was used in the manometer. Experiments were discarded if the spinal fluid contained more than 50 white blood cells per cubic millimeter at the conclusion of the experiment.

Intervals of seven days generally separated experiments upon the same animal. A period of one hour was allowed to establish a control level of pressure. Solutions were then injected intravenously after warming to body temperature. Isotonic fluids were administered during one hour in quantities of 40 to 60 cc. per Kg. Hypertonic solutions were administered, according to the technic of Bullock, Gregersen and Kinney,[3] in quantities of 3.1 Gm. per Kg. of glucose and 6 Gm. per Kg. of sucrose in 50 per cent solutions.

Results.—The cerebrospinal fluid pressure in unanesthetized dogs varied between 75 and 165 Mm. of spinal fluid, as shown in Chart 2. Eighty-one per cent of the determinations fell between 100 and 145 Mm. pressure. The mean pressure was 123 Mm.

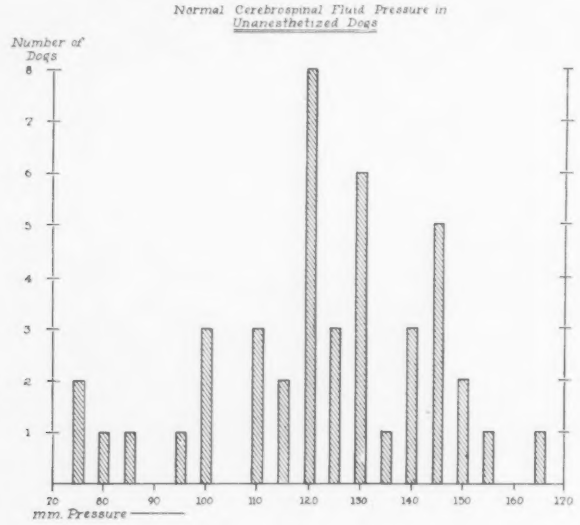

CHART 2.

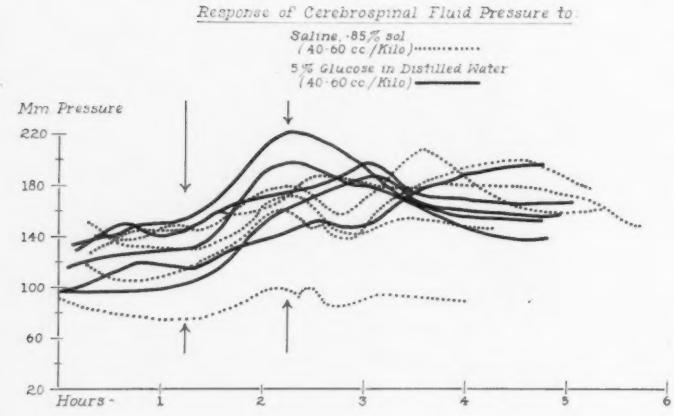

CHART 3.

When isotonic fluids were injected intravenously in quantities of from 40 to 60 cc. per Kg. during a period of one hour, there was an increase in the cerebrospinal fluid pressure as illustrated in Chart 3.

Animals receiving 5 per cent glucose in water excreted 29.1 cc. of urine per Kg., while those receiving the physiologic saline solution excreted 16.1 cc. during the experimental period.

The intravenous administration of 50 per cent solutions of glucose and sucrose produced a fall in the cerebrospinal fluid pressure followed by return to the initial level. No "secondary rise" above the initial level was observed, except in one experiment in which a sucrose solution was used. Chart 4 shows the cerebrospinal fluid pressure changes.

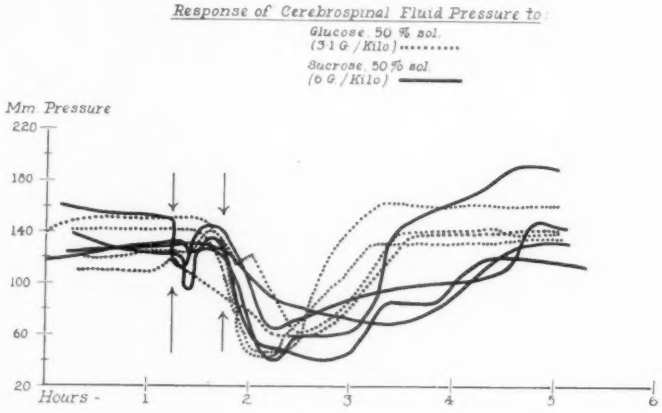

CHART 4.

The diuresis resulting from the injection of the hypertonic sucrose solution averaged 41.2 cc. of urine per Kg., while that for the glucose was 23.7 cc. per Kg. over the period of the experiments.

Discussion.—Hypertonic solutions of glucose and sucrose when injected intravenously caused a temporary fall in the cerebrospinal fluid pressure. A secondary rise above the normal level was observed in only one instance when sucrose was used. These data, therefore, are not in agreement with those of Milles and Hurwitz,[20] who found a "secondary rise" in pressure after the fall produced by the injection of hypertonic glucose solutions. The "secondary rise," they pointed out, was observed only when experiments were prolonged beyond the experimental periods set by other investigators who had not observed the rise. Masserman[17] demonstrated a similar "secondary rise" in observations upon normal humans. Bullock, Gregersen and Kinney[3] suggested using a hypertonic sucrose solution instead of hypertonic glucose, since an undesirable "secondary rise" in pressure occurred only with the latter.

These observers used manometers filled with saline solution to measure the cerebrospinal fluid pressures. Masserman,[16] and Bullock, Gregersen and Kinney[3] encountered not only a "secondary rise" in pressure after the administration of glucose, but also a gradual rise in pressure in control experiments. They did not explain the latter. They demonstrated the presence of large numbers of white blood cells in specimens of cerebrospinal fluid taken at the conclusion of the control experiments and those where glucose and sucrose were used.

In our early control experiments, when saline was used in the manometer, a gradual rise in the cerebrospinal fluid pressure was similarly observed. This variation was attended by the presence of white blood cells in the fluid. We, therefore, used a manometer filled with spinal fluid. With few exceptions, neither a rise in the cerebrospinal fluid pressure nor a pleocytosis was observed. It is possible that the rise in pressure in control experiments and the "secondary rise" following the administration of hypertonic glucose solution, reported by others, is due to the use of saline solution in their manometers. Just what substance in such solutions is responsible for the rise we cannot state at this time.

CONCLUSIONS

(1) The mean cerebrospinal fluid pressure in 43 experiments upon unanesthetized dogs was found to be 123 Mm. of spinal fluid.

(2) When a manometer filled with saline solution was used in unanesthetized, untraumatized dogs, a gradual rise in pressure and pleocytosis was observed. When a manometer filled with spinal fluid was used, with few exceptions, neither a rise in pressure nor pleocytosis occurred.

(3) The intravenous administration of isotonic fluids produced a moderate increase in cerebrospinal fluid pressure over a five-hour period of observation.

(4) Hypertonic solutions of glucose and sucrose, injected intravenously, produced a temporary fall in the cerebrospinal fluid pressure. There was with a single exception no "secondary rise" above the normal level within the experimental period when cerebrospinal fluid was used in the recording system.

II. PHYSIOLOGIC RESPONSE TO THE ADMINISTRATION OF INTRAVENOUS FLUIDS IN DOGS WITH HEAD INJURIES

It has been claimed that increased intracranial pressure is a significant factor in the mortality associated with cerebral injuries.[9, 21] Dehydration of the central nervous system to control the increase in pressure has been proposed as a therapeutic procedure. Fay[9] has presented mortality statistics to support his plan of "dehydration therapy" in cases of cranial injury. Results obtained with this form of treatment, according to Lehman and Parker,[15] were not better than those obtained by others using more conservative methods of treatment. The existence of conflicting views regarding therapy in patients with cerebral injury suggested the need for more information concerning the effect on the cerebrospinal fluid pressure of administering intravenous fluids.

We have studied the effect of the intravenous injection of isotonic and hypertonic solutions and the effect of hydration and dehydration upon the cerebrospinal fluid pressure of the dog with and without cerebral injury. In the course of these studies, certain observations of other phenomena were made. The response of the cerebrospinal fluid pressure to cranial injury was determined; findings relating to recovery or death of the animals were recorded

and correlated; the effect of blood as particulate matter in the cerebrospinal fluid was noted. Since the studies of the cerebrospinal fluid pressure in humans have been made without the use of anesthesia, similar conditions were established in our animals.

Method and Procedure.—Mongrel female dogs, weighing approximately 10 Kg., were used for the experiments. The animals were blindfolded and placed upon the right side for about one hour prior to operative exposure of the left side of the skull. Ether was administered by means of a respirator. The left masseter muscle was reflected from the skull under sterile precautions. The exposed surface was struck four to six blows by means of a steel hammer weighing one and one-half pounds. There occurred a loss of eye reflexes following the trauma, except in two instances. Spontaneous respiration ceased in most cases so that artificial respiration was necessary. The wound was then closed and the anesthesia stopped. Artificial respiration was continued until natural breathing occurred. The animal was again blindfolded, prepared for a cisternal puncture, and catheterized.

With aseptic precautions, a No. 22-gauge needle, one and one-quarter inches in length, was inserted into the cisterna magna after infiltration of the soft tissue with a 1 per cent procaine solution. A specimen of spinal fluid was removed for a count of the red and white blood cells. A manometer of one Mm. bore was attached to the needle in the cisterna and the animal's own fluid allowed to fill the manometer. Six-tenths cc. of fluid was required to fill the system. One hour was allowed for establishing a control level of pressure before the administration of intravenous fluids was begun.

Solutions of 50 per cent glucose in distilled water, 5 per cent glucose in distilled water, and physiologic saline were injected intravenously in quantities of 12 and 40 cc. per Kg. for the hypertonic and isotonic solutions, respectively. Recordings of the cerebrospinal fluid pressure were made every five minutes during the injection period and every ten minutes thereafter. Studies were made on the day of trauma and on subsequent days up to seven days after injury, depending upon the length of survival of each dog. Data recorded included the status of the animal; the cerebrospinal fluid pressure; the character of the cerebrospinal fluid; the response to the intravenous injection of fluids and the quantity of total fluid intake.

Most of the animals which survived the trauma were killed with intravenous sodium amytal one to two weeks following injury. Autopsies were performed on all the animals. Photographs were made of the intact brain and of gross changes present in coronal sections. Specimens were taken for microscopic examination.

Results.—Fracture of the skull was produced in 30 dogs. Blood was present in the cerebrospinal fluid in 23 of these animals. Loss of eye reflexes occurred immediately after trauma in 28. Neurologic disturbances as a result of the trauma were observed in 24. Ten of the dogs died, a mortality of 33 per cent. Table I is a summary of the results of the trauma.

TABLE I

SUMMARY OF THE RESULTS OF TRAUMA

Fractured skull	30
Recovered	20
Died	10
Per cent mortality	33
Loss of eye reflexes	28
Blood in cerebrospinal fluid	23
Residual neurologic disturbances	24

A fairly uniform type of fracture of the skull was produced. The fracture was stellate in character, the line of fracture frequently extending laterally toward the base; there was usually slight depression of the bone underlying the point of impact. In five instances unusual depression of a fragment of bone produced a laceration of the cortex. Gross evidence of injury to the

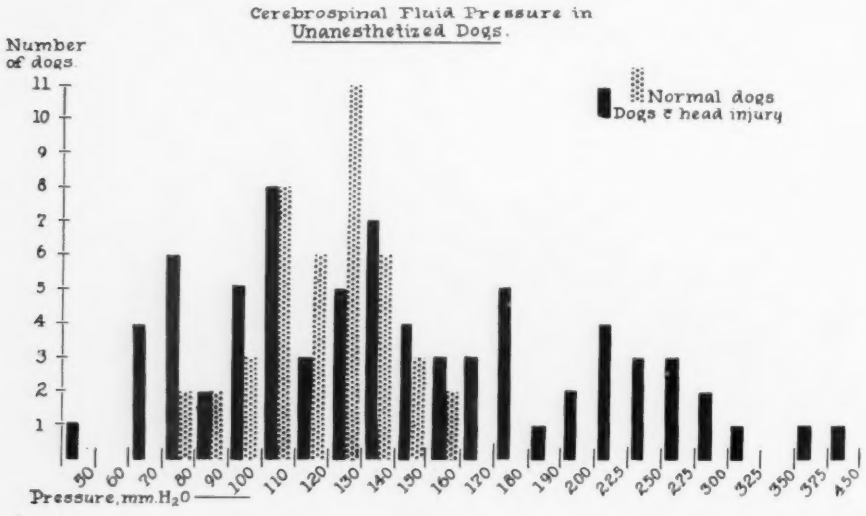

CHART 5.

brain was present in all the animals. The outstanding findings in the brains of the animals that died were subarachnoid and subpial hemorrhages involving the base and brain stem, and punctate hemorrhages in the medulla. Animals that survived showed less severe submeningeal hemorrhage and fine petechial hemorrhages both in and distant from the area of trauma. PLATES I and II indicate the extent of the gross injury which was characteristic of the group of animals that survived in comparison with those that died.

The cerebrospinal fluid pressure of the dogs with head injuries is shown in Chart 5. The recorded pressures were determined in nearly every instance after a one-hour period of observation. In the same chart, pressures previously observed in 43 normal dogs are indicated for comparison. Twenty-eight determinations were made on the day of injury, before the injection of various types of fluid, 19 on the first day after trauma, and 26 at intervals from the second to the seventh day.

The cerebrospinal fluid pressure was less than 200 Mm. of water in 80 per cent of the determinations. In 12 instances, the pressure was between 200 and 300 Mm.; in three, it was above 300 Mm., the highest pressure recorded being 450 Mm. Two deaths occurred in animals which had pressures below 200 Mm. Six deaths occurred among animals having pressures which were above 200 Mm. In the latter instances, severe, diffuse hemorrhage was observed at autopsy. In two instances the animals died immediately after trauma, before the cerebrospinal fluid pressure was recorded.

When isotonic fluids in quantities of 40 cc. per Kg. (corresponding to 3,000 cc. of fluid for a human), were injected intravenously during a period

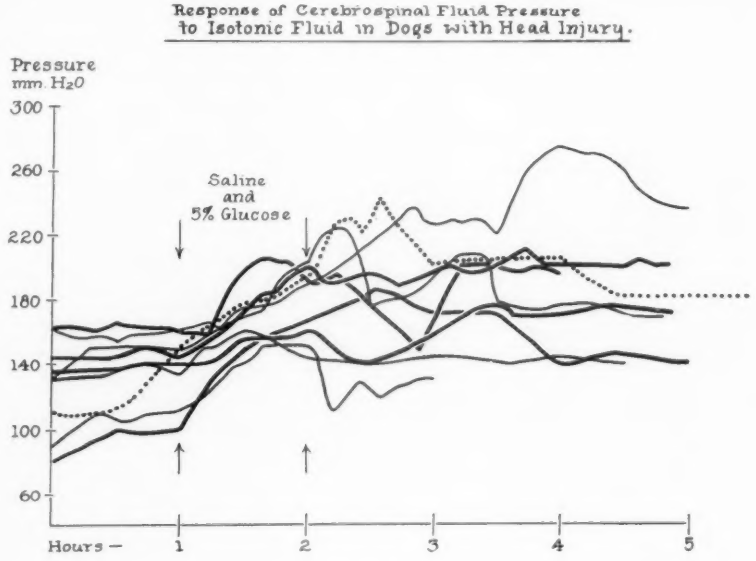

CHART 6.

of one hour, an increase in cerebrospinal fluid pressure was, as a rule, observed, as shown in Chart 6. The final mean increase in pressure was 37 Mm. of spinal fluid. The average urinary excretion of five dogs receiving physiologic saline solution was 16 cc. per Kg. during the experimental period. Normal dogs under the same conditions excreted 16.1 cc. per Kg.

The intravenous administration of 50 per cent glucose solution produced a fall in the cerebrospinal fluid pressure. In no instance was a secondary rise in pressure encountered. Death occurred in two animals following the administration of the glucose solution while the pressure was being measured. In neither case did a rise in the pressure occur. Chart 7 shows the cerebrospinal fluid pressure changes which were observed.

The average urinary excretion in the traumatized group following the injection of hypertonic glucose solution was 22 cc. per Kg. over the period of the experiment. Normal animals receiving 50 per cent glucose solution averaged 23.7 cc. of urine.

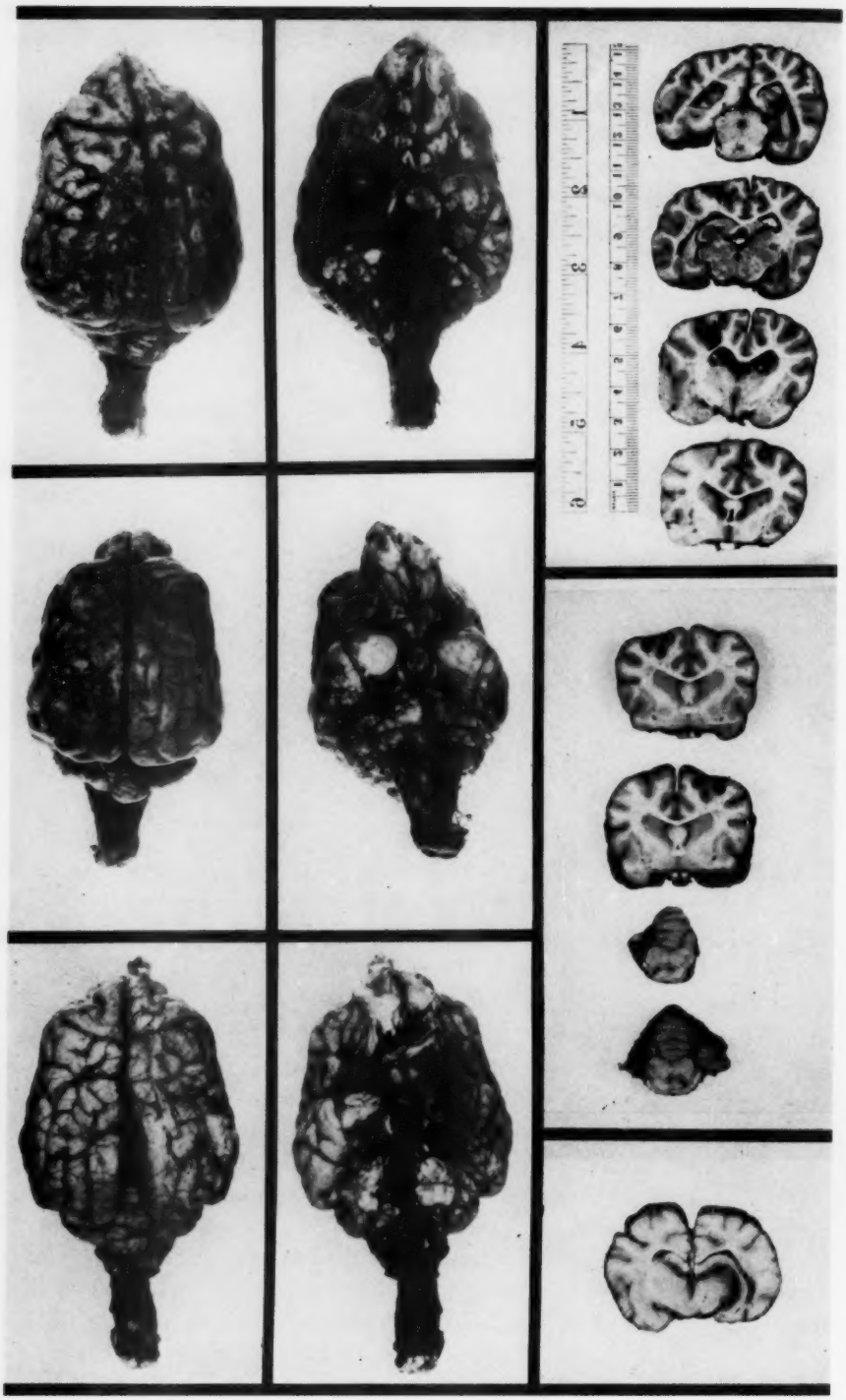

PLATE I

EXAMPLES OF TYPE OF INJURY RESULTING IN MARKEDLY BLOODY CEREBROSPINAL FLUID; INCREASE IN CEREBROSPINAL FLUID, AND DEATH.

Dog No. 92—Pressure 240 Mm.—Glucose experiment
Dog No. 472—Pressure 285 Mm.—Glucose experiment
Dog No. 372—Pressure 450 Mm.—Glucose experiment

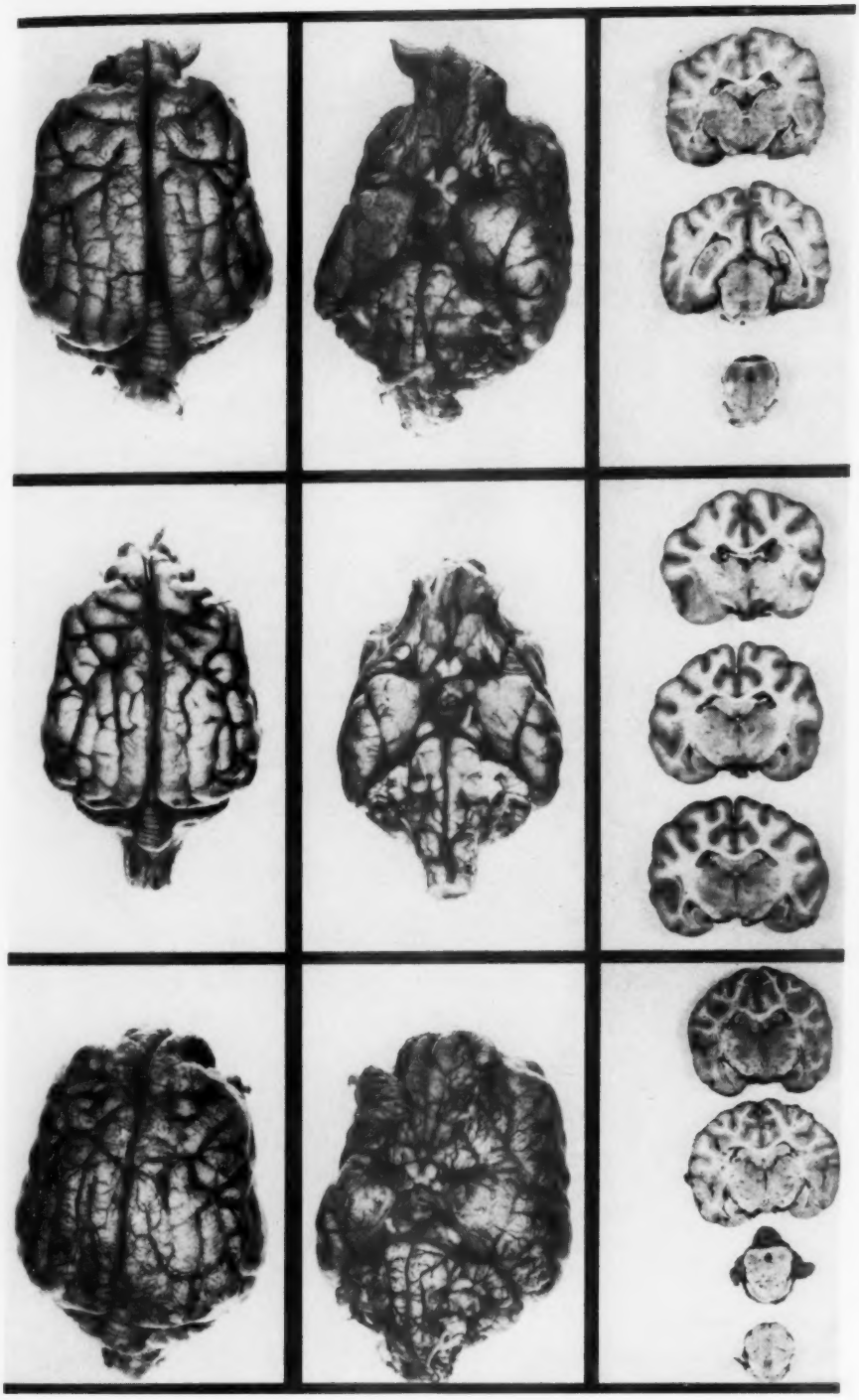

PLATE II

EXAMPLES OF THE TYPE OF INJURY RESULTING IN BLOOD IN THE CEREBROSPINAL FLUID; LITTLE OR NO INCREASE IN THE CEREBROSPINAL FLUID; WITH SURVIVAL.

Dog	Pressure	Experiment
No. 672	140 Mm.	Control
No. 1	165 Mm.	Control
	165 Mm.	Saline
	140 Mm.	Saline
	155 Mm.	Glucose
No. 835	85 Mm.	Control
	85 Mm.	Control

The fluid intake was recorded for all the animals. In a number of instances the quantity of fluid was restricted. In others, a large volume of fluid was administered. Chart 8 shows that there was no correlation between the fluid intake and the cerebrospinal fluid pressure after trauma, in experiments during which the fluid, as a rule, was administered over a prolonged period of time.

Blood was present in the cerebrospinal fluid in 23 of the 30 animals subjected to trauma. Daily counts of the red and white blood cells in the spinal

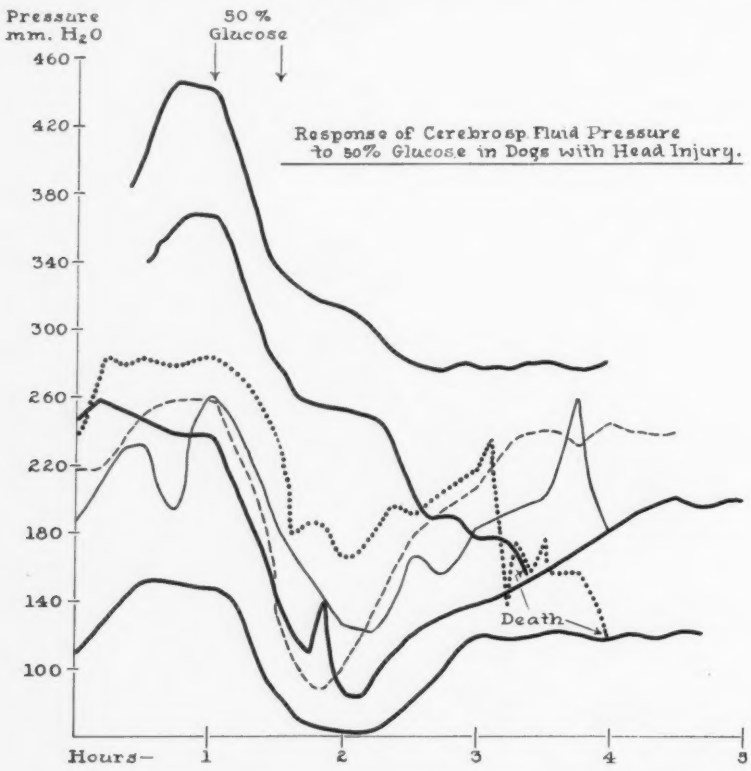

CHART 7.

fluid were made upon nine dogs that survived injury but which showed moderate or markedly bloody fluids. As shown in Chart 9, white blood cells were proportional to red blood cells in the ratio of 1:400, the same as that found in circulating blood. A progressive fall in the number of red blood cells and a proportionate decrease in the number of white blood cells occurred after trauma. Between the fourth and sixth day after injury, the fluid contained up to 40 white blood cells. In one instance, in which a cortical laceration of the brain was produced by the trauma, the number of white blood cells in the cerebrospinal fluid exceeded the proportionate number, as previously described, to a significant degree.

There was a correlation between the amount of blood in the cerebrospinal

fluid and the cerebrospinal fluid pressure when the red blood cells exceeded one million, as shown in Chart 10. All but one of the fatalities occurred in the group of dogs having a high red cell count in the cerebrospinal fluid.

Discussion.—In experiments which have already been reported,[22] the mean cerebrospinal fluid pressure of the normal, unanesthetized dog was found to be 123 Mm. of spinal fluid. In our studies on dogs with head injuries, the mean pressure was 151 Mm., and was less than 200 Mm. in 80 per cent of the experiments. These findings are in agreement with those previously

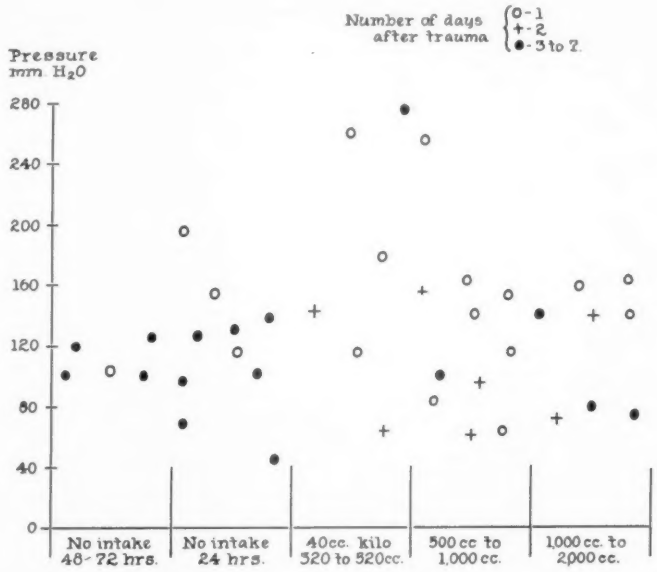

CHART 8.—Illustrating the absence of correlation between the intake of fluid and the cerebrospinal fluid pressure in dogs with head injury. Fluid was administered or withheld over a period of 24 hours, except as indicated. At the end of this period, the cerebrospinal fluid pressure was measured.

reported by Gurdjian, Webster and Sprunk[12] in patients with head injuries. Our observations indicate that the cerebrospinal fluid pressure was not significantly elevated in most instances of cranial injury both in the experimental animal and the human.

No correlation was observed between the fluid intake and the cerebrospinal fluid pressure in dogs with such injuries. In two of the animals all food and water was withheld for 72 hours, with resultant weight loss, and elevation of the serum protein. No significant change in the cerebrospinal fluid pressure occurred.

Dehydration therapy, suggested by Fay,[9] is accomplished by the limitation of fluid intake to 20 ounces of water daily; the use of intravenous glucose solution, and the withdrawal of spinal fluid. Increased intracranial pressure is said to be avoided by these measures. However, the stability of the cerebrospinal fluid pressure may account for the fact that the results of treatment

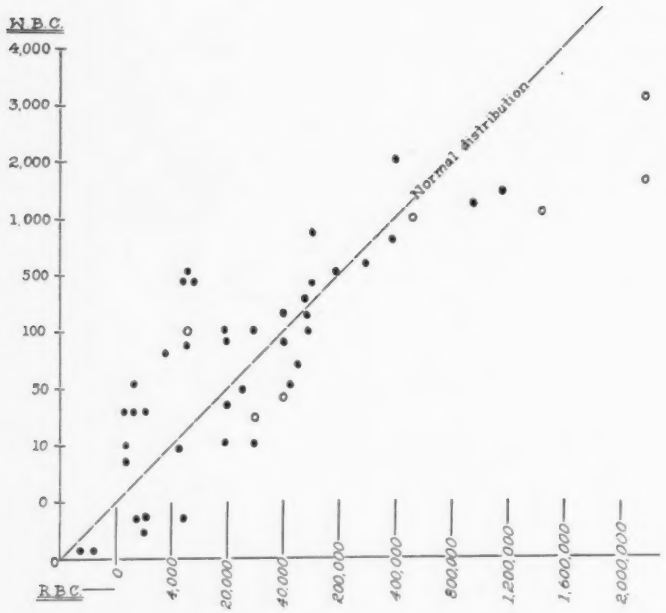

CHART 9.—Illustrating the correlation found between the number of red cells and white blood cells in the cerebrospinal fluids which were bloody after cranial trauma. Counts were made on the day of injury and on subsequent days.

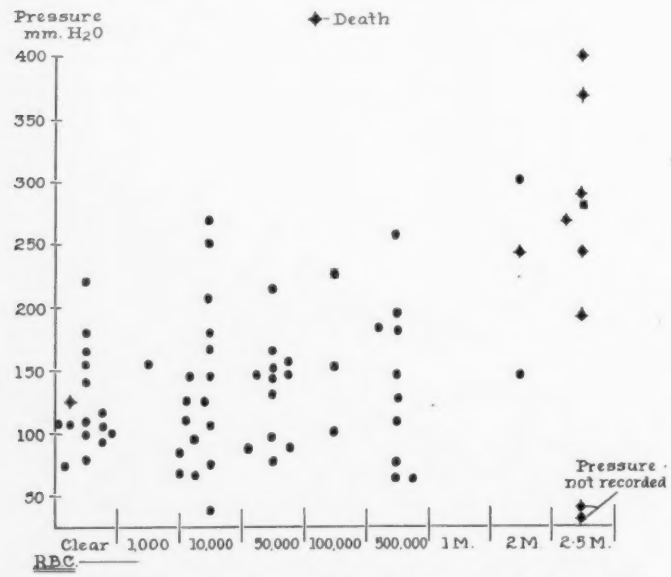

CHART 10.—Illustrating the correlation of death of the animals with the degree of bloodiness of the cerebrospinal fluid, and the cerebrospinal fluid pressure.

of patients with cranial injury by dehydration are no different from those obtained by other methods of treatment.

If it is desirable to lower the increased intracranial pressure, which may or may not be present in cases of cerebral trauma, the question may be raised as to the effectiveness of restriction of fluid to accomplish this end. On the other hand, it does not appear reasonable to fear that an adequate intake of fluid will have an unfavorable effect upon the patient by significantly increasing the intracranial pressure.

The injection of 50 per cent glucose solution intravenously in animals with the severest head injuries, and with the highest cerebrospinal fluid pressure which we encountered, resulted in a fall of the pressure in each instance. No secondary rise in pressure was observed. Browder,[2] Jackson,[14] and others have reported a secondary rise in pressure following the administration of 50 per cent glucose solution to humans with cranial trauma.

No meningeal reaction as indicated by an increase in the number of white blood cells in the cerebrospinal fluid was observed to be caused by blood in the cerebrospinal fluid. Essick,[8] in experiments showing the reaction of the arachnoid to particulate matter, found that blood injected into the subarachnoid space produced a marked pleocytosis. Weed[25] restated the findings of Essick, and described further experiments dealing with the effects of other particulate matter. Bagley[1] showed significant late pathologic changes resulting from the injection of blood into the cerebrospinal fluid.

Our findings differ from those of Essick, but agree with observations made by Merritt and Fremont-Smith.[19] The latter noted that in 26 cases of subdural hematomata, with blood in the spinal fluid, the number of white blood cells was, with few exceptions, proportional to the number of red blood cells.

A reason for the above discrepancy in findings may be found in the experimental technic employed by Essick, which consisted in laking blood with distilled water. Sodium chloride was then added to make an isotonic solution before it was injected into the cisterna of the animal. The injection of this solution resulted in a "sterile meningitis" within a few hours. In our experience, the injection of physiologic saline solution into the cisterna, or even the use of saline solution in a manometer to measure the cerebrospinal fluid pressure, results in a reaction similar to that encountered by Essick. The effect of saline solution in a manometer to measure the cerebrospinal fluid pressure has been reported upon in a previous publication.[22]

Doubt has arisen as to the etiologic significance of increased intracranial pressure in deaths due to head injury. From the experimental standpoint, the cerebrospinal fluid pressure must equal or exceed the diastolic blood pressure in order to produce profound effects upon the organism.[5] Cerebrospinal fluid pressure in such a range has not been observed.[4, 12] From the clinical standpoint, operative treatment aimed at the relief of increased intracranial pressure in patients with fractured skulls has been found to be unnecessary and even dangerous. Dehydration therapy has not yielded striking

benefits in clinical cases. The rationale of treatment based upon reduction of the intracranial pressure may, therefore, be questioned.

Two additional relationships may be of greater significance: First, the degree of bloodiness of the cerebrospinal fluid was found to be closely correlated with the death of the animals in our experiments. Of ten animals that died following injury, nine had markedly bloody cerebrospinal fluid containing one to five million red blood cells. A second correlation was found between the quantity of blood in the cerebrospinal fluid and the increase in the cerebrospinal fluid pressure that occurred. The greater the degree of bloodiness of the spinal fluid, the higher was the cerebrospinal fluid pressure, as shown in Chart 10. Deaths, therefore, might have occurred not because of the increased intracranial pressure itself but rather as a result of the severity of the brain injury as reflected by the quantity of blood in the cerebrospinal fluid. In our opinion, treatment directed merely toward removing the red blood cells from the cerebrospinal fluid or reducing its pressure, incidents resulting from the cerebral damage, is of questionable value.

CONCLUSIONS

Dogs which sustained severe head injuries were found to have cerebrospinal fluid pressure which were less than 200 Mm. in 80 per cent of the cases, and more than 200 Mm. in 20 per cent.

The intravenous administration of isotonic fluids produced a moderate increase in the cerebrospinal fluid pressure. The state of hydration or dehydration, as indicated by fluid intake, had no significant effect on the cerebrospinal fluid pressure after head injury.

Fifty per cent glucose solution administered intravenously lowered the cerebrospinal fluid pressure in all instances. No secondary rise in pressure was observed.

The presence of blood in the cerebrospinal fluid following head injuries in dogs did not produce an increase in the number of white blood cells above the proportionate number.

When the cerebrospinal fluid contained red blood cells, amounting to two million or more, the cerebrospinal fluid pressure was elevated, and the mortality was 75 per cent.

The ultimate outcome of dogs with head injuries was more clearly correlated with the degree of damage to the nervous system, expressed by the presence of blood in the cerebrospinal fluid, than with the elevation of the cerebrospinal fluid pressure.

The authors wish to express their appreciation for the assistance accorded them by Miss Elizabeth Thorogood and Dr. C. C. Miller, and for the suggestions and cooperation of Drs. I. S. Ravdin and F. C. Grant.

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THE INDUCTION OF LIVER NECROSIS IN RABBITS BY THE COMBINATION OF EXPERIMENTAL HYPERTHYROIDISM AND SHOPE PAPILLOMA

W. C. Sealy, M.D.

Durham, N. C.

FROM THE DEPARTMENT OF SURGERY, DUKE UNIVERSITY SCHOOL OF MEDICINE, DURHAM, N. C.

The influence of hyperthyroidism in the morphologic and physiologic alteration of the liver has long been recognized. Habersohn,[1] in 1874, noted jaundice in patients with hyperthyroidism. Marine and Lenhart,[2] in a study of pathologic anatomy of the toxic goiter, called attention to scarring of the liver in this disease. Barker[3] reported a case of advanced central necrosis in the liver of a patient dying from hyperthyroidism. In 1932, Weller[4] cited the hepatic changes in 48 cases of Graves' disease in which all other possible causes of damage were excluded. He described marked chronic hepatitis in 26 cases, slight chronic hepatitis in 16, and no lesions in six. Beaver and Pemberton,[5] in 1933, collected 107 cases of hyperthyroidism coming to autopsy at the Mayo Clinic, describing in the liver: (1) Acute degenerative changes; (2) simple atrophy; and (3) subacute toxic atrophy and toxic cirrhosis. Cameron and Karunaratne[6] reported 30 cases of hyperthyroidism and observed the hepatic changes described by other authors.

Clinical evidence of disturbed liver function in hyperthyroidism has been reported by many authors. Youmans and Warfield,[7] using the phenoltetrachlorphthalein test, found hepatic damage in 22 of 44 persons who had hyperthyroidism. Maddock, Coller and Pederson[8] reported eight out of 13 cases of toxic goiter with evidence of liver damage, as tested by serum bilirubin and bromsulphalein determinations. Bartels[9] reported 148 cases of hyperthyroidism that were subjected to the Quick hippuric acid test, and all but 18 showed evidence of impaired liver function.

The experimental production of liver necrosis has been attempted by many workers. Farrant,[10] in 1912, described central fatty changes in liver of cats and rabbits that were fed desiccated thyroid until death was produced. In 1921, Hashimoto,[11] while working with rats and studying the effect of desiccated thyroid on heart muscle, described central necrosis of the liver. It is interesting that the incidence of pneumonia in his group of animals was 85 per cent, but no attempt was made to correlate this complication with the cardiac or hepatic changes. Gerlei,[12] in 1933, and Sciaky,[13] in 1936, described liver necrosis in rabbits following the injection of thyroxin. Goodpasture,[14] in 1921, while studying the effect of experimental hyperthyroidism induced by thyroxin and desiccated thyroid on the heart muscle of rabbits, in combination with chloroform inhalation, did not observe any necrosis of liver with thyroxin alone or in combination with small amounts of chloroform. Cameron and Karunaratne,[6] using rats, were not able to produce liver necrosis

Submitted for publication July 2, 1940.

with thyroxin. Davis and Whipple[15] could not detect any increased necrosis when desiccated thyroid was fed to animals along with chloroform. Haban,[16] in 1935, fed rabbits desiccated thyroid and thyroxin, and called attention to the presence of central necrosis in four out of seven rabbits, all four having an acute intercurrent infection. He concluded that a combination of hyperthyroidism and infection was necessary to cause liver necrosis. The necessity of a factor other than hyperthyroidism in the production of lesions of the heart muscle has been demonstrated by Goodpasture,[14] using thyroxin and chloroform, and by Schultz,[17] using thyroxin and desiccated thyroid plus a chronic streptococcic infection.

In a further study to determine the effects of experimental hyperthyroidism on the liver, rabbits having sloughing infected skin tumors (Shope papillomata) were used, and widespread central necrosis was found. This change in the liver could not be produced by experimental hyperthyroidism in normal rabbits, nor was it present in rabbits having only Shope papilloma and not fed desiccated thyroid. A report of this study follows.

In this investigation 41 rabbits were used. The first group consisted of rabbits presenting multiple sloughing infected skin tumors resulting from infection with the Shope papilloma virus and in which hyperthyroidism was produced by desiccated thyroid; the second group were normal stock animals given desiccated thyroid in exactly the same manner as Group I; and the third group showed skin lesions similar to Group I and were killed, as controls, without the administration of desiccated thyroid.

Armour's desiccated thyroid, U.S.P., prepared in 0.128 Gm. tablets, was used throughout the experiment; the tablets being fed either dry or in a suspension of tap water each evening. The use of desiccated thyroid has been employed by many workers and found to induce experimental hyperthyroidism,[10, 16, 17] with the weight loss being a satisfactory index of the degree of toxicity.[10, 16] The rabbits were all kept in separate cages and fed a diet of cabbage, oats, and rabbit chow.

Except in the ones indicated in Table II, all the thyroid-fed rabbits were allowed to die or to reach such a critical stage that it was deemed advisable to kill them. The sections were fixed with Zenker's solution and stained with hematoxylin and eosin.

The control papilloma animals were sacrificed by either a blow on the head or by injection of air into the ear vein, with the tissues fixed and stained in the same manner already described.

The Shope papilloma is a cutaneous "warty" growth that is easily induced in domestic rabbits by a virus isolated from wild rabbits.[18] The behavior of the tumor on the host is typical of any rapidly progressive new growth on the body surface in that its size soon exceeds the blood supply; and, as a sequela of this as well as a result of trauma, necrosis and secondary infection follow. The effect of the tumor on the host is not marked except in the occasional growth that progresses to malignancy as has been reported by Rous and Beard.[19] From eight to 12 weeks before these experiments were begun the rabbits used in Groups I and III had received multiple skin inoculations with

the purified virus protein derived from the Shope papillomata during an experiment conducted by Drs. W. R. Bryan and J. W. Beard.[20] Following these inoculations, from five to 15 papillomata developed on each animal, measuring from 3 to 5 cm. in diameter, all showing some necrosis and secondary infection.

GROUP I.—There were 15 domestic rabbits that had been inoculated with the Shope papilloma virus, as described, in which experimental hyperthyroidism was produced by desiccated thyroid. Table I shows the initial weight, the weight loss, the amount of desiccated thyroid given per day, the number of days the preparation was administered, and the survival period of each animal.

TABLE I

SUMMARY OF RABBITS INFECTED WITH SHOPE PAPILLOMA VIRUS RECEIVING DESICCATED THYROID

Rabbit No.	Condition at Beginning of Experiment	Amt. of Desiccated Thyroid per Day in Gm.	No. of Days Fed Desiccated Thyroid	Days Before Death	Wt. in Gm. Beginning of Experiment	Wt. Loss in Gm.	Liver Changes	Other Changes
918	Fair	0.128	6	7	2,400	350	++++	Pneumonia
917	Fair	0.128	32	33	2,075	600	0	0
921	Fair	0.512	14	15	2,250	925	++++	Pneumonia
943	Poor	0.512	2	3	2,100	375	++++	Pneumonia
914	Fair	0.768	8	9	2,050	600	0	0
969	Good	0.768	6	7	2,600	575	+++	0
1242	Good	0.768	6	7	1,900	450	+	0
1249	Poor	0.768	2	3	1,500	250	+++	0
1252	Good	0.768	3	4	2,100	350	+++	Purulent pericarditis
1839	Good	0.768	3	4	1,850	350	++	0
1885	Good	0.768	3	4	2,125	375	++	0
2005	Good	0.768	2	3	2,100	400	+	0
2278	Good	0.768	6	7	1,850	450	+	0
2267	Good	0.768	5	6	2,250	500	++++	0
2276	Fair	0.768	3	4	1,650	200	0	0

Twelve of the 15 animals in this group showed liver necrosis, central in type, with an occasional involvement of the midzonal area. This was accompanied by cellular infiltration. The extent of the process varied from small areas around the central vein to two-thirds of the liver lobule. The microscopic picture was no different from that seen in necrosis from other toxic agents. A description and photomicrographs of sections from the livers of two rabbits are included.

Rabbit No. 943.—The microscopic study of the liver shows widespread central necrosis with an occasional area of midzonal involvement accompanied by slight cellular infiltration. A minimal amount of fatty change is present in some locations. Passive congestion and changes about the portal areas are not present (Fig. 1).

Rabbit No. 1839.—Except for the degree, the microscopic changes are essentially the same as in Rabbit No. 943. The necrosis is in the same location but not nearly so extensive, while the cellular infiltration is much more extensive (Fig. 2).

In grading the degree of necrosis present in the livers of the rabbits in Group I, the designations one plus, two plus, three plus, and four plus were used. Fig. 1 illustrates the change classified as four plus, and Fig. 2 that classified as two plus.

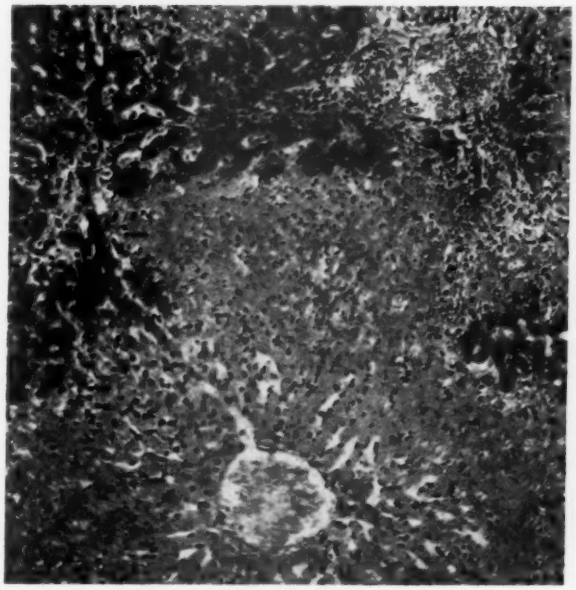

FIG. 1.—Rabbit No. 943: Photomicrograph showing widespread necrosis of the liver in rabbits presenting multiple necrotic and infected skin tumors (Shope papillomata) three days after the induction of experimental hyperthyroidism (×150).

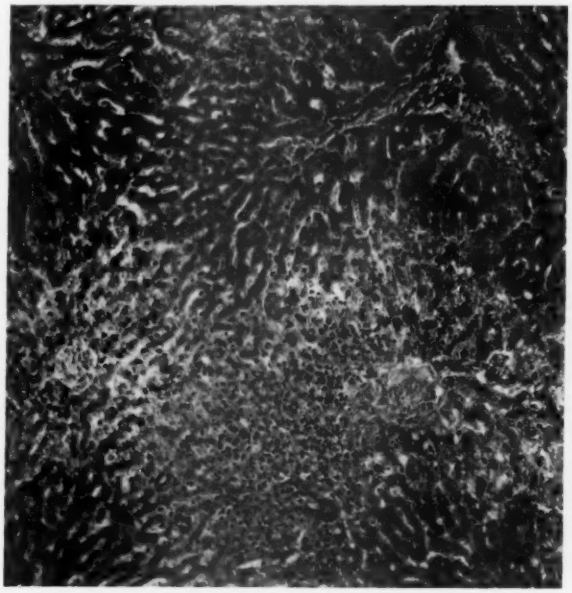

FIG. 2.—Rabbit No. 1839: Photomicrograph showing central necrosis of the liver with polymorphonuclear infiltration in a rabbit presenting multiple necrotic and infected skin tumors (Shope papillomata) four days after the induction of experimental hyperthyroidism (×150).

GROUP II.—Fifteen normal rabbits were in this group. Hyperthyroidism was produced exactly as in Group I. With the exception of the three rabbits killed at the end of three days and two rabbits killed at the end of two days, without regard to their general condition, all were allowed to die from the effects of the desiccated thyroid. Four rabbits of this group received 20 cc. of 20 per cent ethyl alcohol daily by mouth in addition to the desiccated thyroid. None of the livers in this group showed any significant changes. The data are summarized in Table II.

TABLE II

SUMMARY OF NORMAL RABBITS FED DESICCATED THYROID

Rabbit No.	Condition at Beginning of Experiment	Amt. of Desiccated Thyroid per Day in Gm.	No. of Days Fed Desiccated Thyroid	Days Before Death	Wt. in Gm. Beginning of Experiment	Wt. Loss in Gm.	Liver Changes	Other Changes
238	Good	0.128	32	33	2,075	600	0	0
237	Good	0.512	21	22	2,100	825	0	0
239	Good	0.768	11	12	1,900	775	0	0
406	Good	0.768	6	7	2,200	725	0	0
409	Good	0.768	13	14	1,850	475	0	0
403	Good	0.768	15	16	2,100	675	0	0
402(A)*	Good	0.768	3	4	2,000	150	0	0
405(A)	Good	0.768	3	4	2,300	250	0	0
408(B)†	Good	0.768	3	4	1,725	175	0	0
401(B)	Good	0.768	6	7	1,875	400	0	0
404(B)	Good	0.768	6	7	1,800	325	0	0
3(C)‡	Good	0.512	5	6	2,000	500	0	0
4(C)	Good	0.512	8	9	2,050	650	0	0
5(C)	Good	0.512	9	10	2,675	725	0	0
6(C)	Good	0.512	8	9	2,275	1,025	0	0

*(A) Killed at end of four days without regard to general condition.
†(B) Killed at end of seven days without regard to general condition.
‡(C) In addition to desiccated thyroid received 20 cc. of 20 per cent ethyl alcohol per day.

GROUP III.—Eleven rabbits having Shope papillomata, in all respects similar to those in Group I but not fed desiccated thyroid, were killed as controls to determine if the papillomata alone had any effect on the liver. In no case was there any change other than an occasional focal area of fatty change (Table III).

Discussion.—These experiments demonstrate that liver necrosis can only be produced with desiccated thyroid when there is a second factor present, in this instance the Shope papilloma. This conception of the summation or combination of factors is not new, as Opie,[21] in 1910, noted that the combination of small amounts of either chloroform or phosphorus with intravenous injections of bacteria produced profound liver necrosis beyond that expected from either factor alone. Desiccated thyroid is capable of producing a marked rise in the metabolism of cells, and this increase can be carried to the point of exhaustion, as illustrated in Group II where normal rabbits were used. That this is not sufficient to induce cellular necrosis is clearly shown in the postmortem studies of Group II.

The Shope papilloma is a skin tumor that in this experiment was allowed to reach considerable size and to remain on the host for two to three months. During this time necrosis and secondary infection had resulted. It is prob-

able that products from tumor tissue necrosis and bacterial infection are absorbed; but as shown in Group III, these products do not affect the microscopic appearance of the liver.

TABLE III

SUMMARY OF RABBITS PRESENTING SHOPE PAPILLOMATA AND NOT RECEIVING DESICCATED THYROID

Rabbit No.	Liver Changes	Other Changes
1247	0	0
1269	0	Paralysis of bladder Marked cystitis
1245	0	0
1240	0	0
1893	0	Pneumonia
1895	0	0
2001	0	0
2003	0	0
2279	0	0
2270	0	Pneumonia
2077	0	0

The second factor is not the virus itself as the extracts from these papillomata on domestic rabbits are not infectious,[18] nor could Beard and Wyckoff[22] demonstrate the virus protein in the tumor extracts by the ultracentrifuge. Thus it is suggested that products resulting from papillomata, whether from tumor necrosis or infection, combined with the increased metabolism cause liver necrosis. It is possible that the metabolism of the cells is thus so greatly stepped-up that the point of exhaustion is reached, and substances once easily detoxified by the liver, now are capable of producing cellular necrosis.

In addition to the necrosis and infection in the papillomata, four of the 15 rabbits in Group I had an acute intercurrent infection; and in each of these the liver showed extensive necrosis. On the other hand, in the control papillomata group three animals with intercurrent infections in addition to the papillomata did not show significant liver changes. This suggests that the liver necrosis produced by the combination of hyperthyroidism and the Shope papillomata is increased by presence of an acute infection.[16]

Another interesting point is the relation of the liver necrosis and the decrease of liver cell glycogen caused by experimental hyperthyroidism. This glycogen loss renders the cell more susceptible to any toxic agent, which in this case may be products of necrosis and infection from the papilloma.

The clinical significance of the above is evident when one considers that in deaths from hyperthyroidism there is often a complicating factor, such as (1) anesthetic agents with or without accompanying anoxemia; (2) an acute intercurrent infection; and (3) the absorption from the operative site of the products resulting from trauma and bacterial contaminants. One or more of these factors combined with hyperthyroidism may well account for cases of liver necrosis observed by authors reporting human autopsy material. Further work on this subject is now in progress.

CONCLUSIONS

(1) Liver necrosis was produced in 12 of 15 rabbits having necrotic, infected, cutaneous "warty" growths (Shope papillomata) by experimental hyperthyroidism induced with desiccated thyroid.

(2) Liver necrosis was not present in 15 normal rabbits after a similar degree of hyperthyroidism had been produced with desiccated thyroid.

(3) Liver necrosis was not present in 11 rabbits having necrotic, infected, cutaneous "warty" growths (Shope papillomata) in which hyperthyroidism was not induced.

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PERINEAL PROSTATOTOMY AND PROSTATECTOMY FOR THE REMOVAL OF PROSTATIC CALCULI*

ROBERT GUTIERREZ, M.D.
NEW YORK, N. Y.

CALCULI of the prostate have been known from the early days of modern medicine, and their existence has raised problems with reference to both the diagnosis and treatment. With the advent of radiography, and especially of urography, their shadow-casts became familiar to urologists, and their diagnosis was lifted out of the obscurity in which it was formerly enshrouded. In the last few decades, these calculi have accordingly received considerable attention in the medical literature, which has revealed that they are far more common than had been believed. In fact, in routine postmortem examination, prostatic calculi of one type or another have been found by pathologists in approximately one out of every five individuals over 50 years of age, indicating that the condition of prostatolithiasis is pathologically very common. That they constitute an important chapter in the study of urology cannot be denied. The fact that great numbers of such stones run a symptomless course over a long period of time in no way detracts from their importance, since it is now recognized that the presence of a stone means the presence of infection, which tends sooner or later to excite inflammation and obstructive symptoms, as well as to serve as a focus for dissemination of pathogenic bacteria to other organs of the body.

Etiologically, these prostatic calculi fall into two distinct classes—the endogenous and the exogenous. *Endogenous* prostatic calculi develop primarily within the substance of the prostate gland, from slow deposit of calcium salts around the corpora amylacea found normally within the acini and tubules of the prostate. Just as these corpora are now known to be more abundant in men over the age of 50, it is likewise true that endogenous prostatic calculi are more commonly found in the later years of life, often in association with parenchymal prostatitis or adenomatous prostatic hypertrophy. In fact, during a perineal prostatectomy for such hypertrophy, it is quite common for the knife to encounter minute, multiple concretions that have not been previously suspected. The growth of such calculi is stimulated if they are so situated that urine has access to them, and they then tend to give rise to prostatic abscess and possible fistula or the formation of diverticula. In the group of *exogenous* prostatic calculi, on the other hand, are included those cases of the entire region of the prostatic urethra, in which a stone already formed in the upper part of the urinary tract enters the urethra and becomes wedged within the body of the prostate, lodged within one of its ducts or crypts, or in a diverticulum already present. Constant bathing with the urine as it escapes from the

* Read before the annual meeting of the American Urological Association, White Sulphur Springs, W. Va., June 1, 1939. Submitted for publication August 16, 1939.

bladder accelerates the growth and rapid development of these stones. It is possible also to recognize a *mixed* group of stones, which, beginning within the prostate, as endogenous, find their way through the mucosa of the urethra, and then become lodged where the urine contributes an exogenous element in the form of urinary salts, encouraging their growth and formation to such an extent that they may paradoxically be termed *endo-exogenous* prostatic calculi. The chemical analysis of such a stone will show that, while the outer covers or layers are of urinary salts, the nucleus is formed of the primary elements of the corpora amylacea.

Irrespective of their origin, all stones that are producing symptoms within the urinary tract call for surgical relief. The diagnosis is made on the basis of the roentgenographic and urographic findings, in conjunction with rectal and urethrocystoscopic exploration. When it becomes evident that the symptoms within the urinary tract are attributable to the presence of prostatolithiasis, *all stones within the region of the prostatic urethra fall, for practical purposes of treatment, into a single group.* All stones producing symptoms demand surgical removal. In the overwhelming majority of cases, such removal should be carried out by the perineal route. In some cases, however, other avenues of approach, such as the suprapubic or the transurethral operation may be indicated. Occasionally stones associated with obstructing median bars, lying close to the surface of the mucosa of the prostatic urethra, may call for endoscopic prostatic resection, but in most cases of multiple calculi the stones do not lie within the region that can be reached by this procedure, and many calculi are sure to be overlooked. A prostate full of stones can only be reached satisfactorily by way of the perineum, where the choice of operation will lie between perineal prostatotomy and perineal prostatectomy. A detailed discussion of their surgical management and their operative indications and results is herewith presented, with a view to offering a plea in behalf of a more extensive employment of open operative treatment in well-selected cases of this type of lithiasic disease (Fig. 1). It will be seen, from the various types of calculi of the prostate that I am exhibiting, what a wide range of possibilities in the mode of formation these cases may present. However, all alike demonstrate the superior advantages presented by the perineal approach when the choice of an operation is to be made. They also show the importance of an accurate preoperative diagnosis and the necessity of applying the correct surgical procedure to each individual case, in order to reach a sound prognosis and to obtain a permanent cure.

The purpose of this communication is, therefore, to report a series of 29 cases of prostatolithiasis that have come under my personal observation and to discuss briefly this important subject, in the hope of stimulating further studies and research in this field.

Up to the end of the sixteenth century only the most vague ideas existed with reference to prostatic calculi. The first definite reference to the subject is found in the writings of Marcellus Donatus,[11] who, in 1586, reported that he had observed a stone in the prostate of one of his patients which caused an

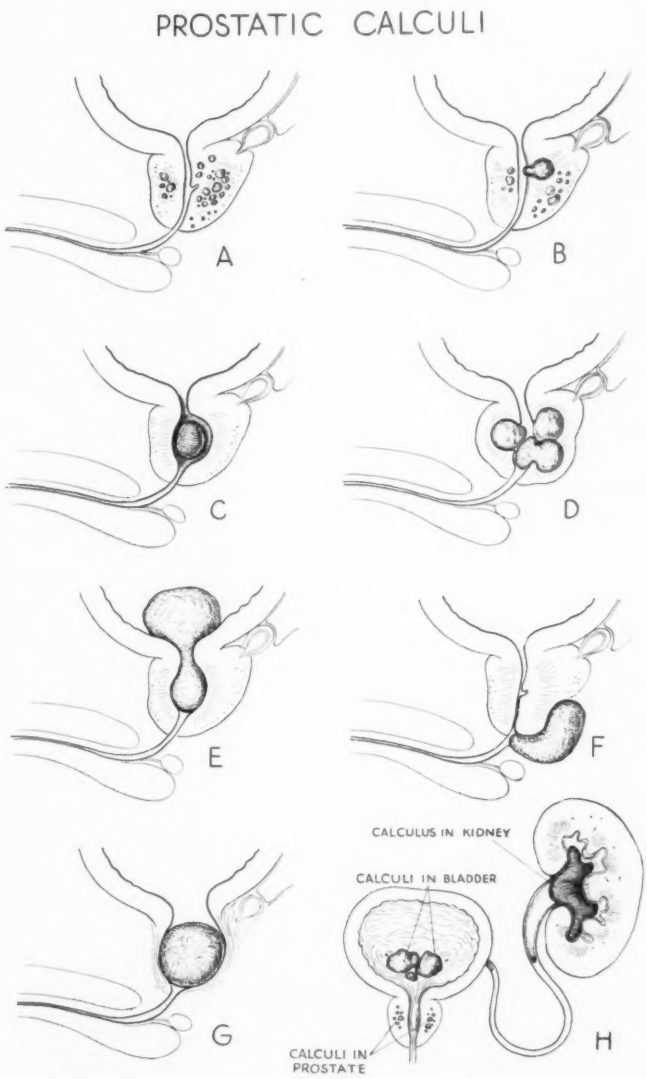

FIG. 1.—Schematic drawing to illustrate the different types of prostatic calculi: (A) Multiple prostatic calculi of endogenous origin within the body of the prostate and having no connection with the urinary tract. (B) Represents the conception of a mixed endo-exogenous calculus within the prostate, in which one of the endogenous calculi has ruptured through the mucosa of the urethra where it meets the exogenous elements of the urine, accelerating its growth. (C) A prostatic stone, coming from the upper urinary tract, has become embedded in the region of the prostatic urethra. (D) Multiple calculi have formed in a diverticulum resulting from the rupture of a prostatic abscess. (E) A prostato-urethrovesical calculus impacted in the vesical neck, producing marked obstruction to the outflow of the urine. (F) A paraprostatic calculus occupying a diverticulum of the membranous urethra at the apex of the prostate, and encroaching upon the gland. (G) Prostatic calculus formed in the region of the prostatic urethra after prostatectomy. (H) Prostatolithiasis associated with vesical calculi and nephrolithiasis.

obstruction to the secretions of the organ. In 1619, Fabricius Bartoletus[3] recorded a case of complete urinary retention in a patient who had a stone "formed by retained sperm," which made pressure upon the neck of the bladder. In 1707, Jacobus Douglas[12] reported the case of an aged man in whom he had found some small, hard, white bodies resembling peas of stony consistency. They presented a polished appearance on their external aspect: "Some of them were situated in the prostate itself, while others were attached by small rootlets to the covering membrane of the gland." In the same year Frederic Lessius[30] wrote of a stone that blocked the canal of the prostate into the urethra, causing sterility.

Not until 30 years later, however, did anything that could be called definite appear on the subject when Pohl,[46] in 1737, gave the first description that was of any real value, in a work entitled, "Prostates affectées d'un calcul," in which he made a serious study of the condition. This was followed by allusions to the subject by Louis,[3] in 1747, in his "Mémoires sur les pierres urinaires," and by Morgagni,[41] in 1762, the latter author giving a description of small prostatic stones that is still regarded as a classic. During the early part of the nineteenth century prostatic stones were discussed by Home,[23] Amussat,[2] and Marcet and Civiale,[7] none of whom, however, appears to have had any very clear ideas on the subject, either with reference to their etiology or to the organic changes to which they may give rise. After Vidal de Cassis[58] and Velpeau[57] had given some study to these calculi, Leroy d'Etiolles[32] reported a number of cases, upon which he operated by a special "urethrolithotritor" devised for the purpose of crushing stones in the prostate. In the latter half of the century several French theses were published, notably those of Bernard[4] (1857), Mélisson[37] (1873), Malteste[34] (1876), and Ménagé[38] (1880). In England, H. Thompson[55] (1861) found space for a chapter on the subject in his treatise on diseases of the urinary tract.

At the close of the nineteenth century, the subject received scientific consideration in the works of Guyon,[20] Albarran,[1] Legueu,[29] and Pasteau,[45] all of whom have discussed at length the pathogenesis and treatment of these calculi. In 1901, the whole subject was reviewed and brought up-to-date in the comprehensive thesis of Tarnaud,[53] which included reports of 51 cases found in the literature. Calculi of the prostate proper (endogenous) and calculi of the prostatic urethra were distinguished, and a detailed study made of their pathologic anatomy, pathogenesis, diagnosis and treatment.

Within the current century, since radiography and, later, urography have become routine methods of examination, the subject has received the attention of many leading urologists. Important contributions have been written by Young,[62] Kretschmer,[28] Judd and Crenshaw,[27] Thomas and Robert,[54] Judd, Parker and Morse,[26] G. J. Thompson,[56] Moore[39, 40] and others; in England the subject has been discussed by Joly,[25] White,[61] and Thomson Walker;[60a] in Germany by Virchow,[59] Englisch,[13] Gläsel,[15] Posner,[46a] and others; and in France by Pasteau,[45] Delauney,[10] Gayet,[14] Oraison,[44] Pousson,[47] and Corlineau.[9]

From time to time, histologic examinations of large series of prostates removed at autopsy have been reported in the literature by various authors, from which it became evident that the presence of prostatic calculi is relatively common. Recently Randall[49] published a monograph on the surgical pathology of prostatic obstructions in which he stated that in routine autopsy specimens of 324 subjects, 86, or 26.5 per cent, were positive for prostatic calculi, which indicates a hitherto unsuspected frequency of this type of pathology.

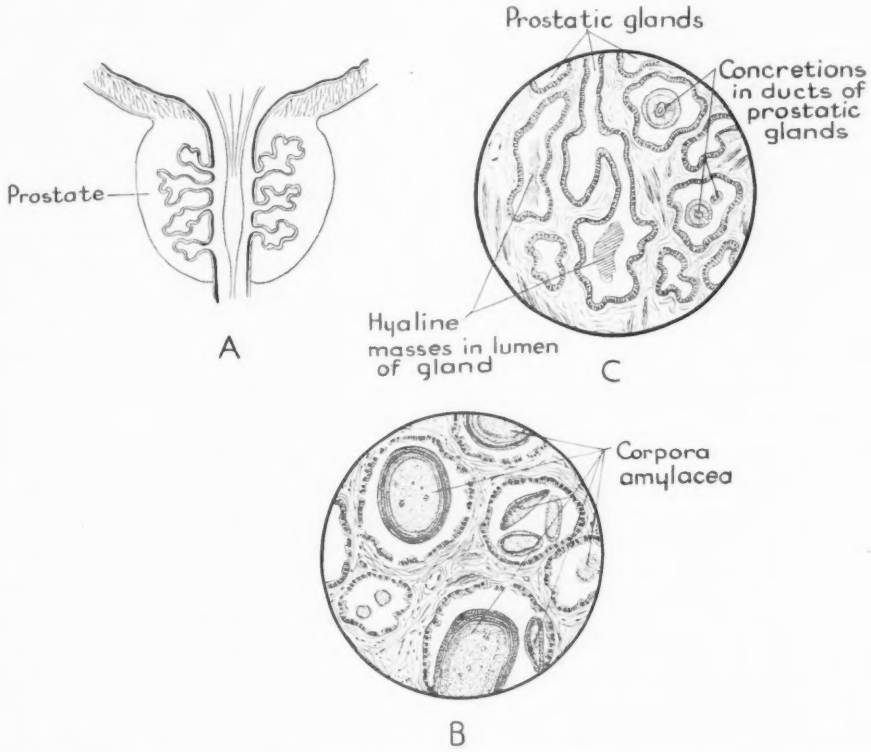

FIG. 2.—Schematic drawing to illustrate the etiology of endogenous prostatic calculi: (A) Transverse section of prostate, showing the racemose structure of the organ. (B) Drawing from a histologic section of the prostate showing the presence of multiple corpora amylacea in the acini of the gland. (High power). (C) Drawing of another section showing hyaline masses in the lumina of the gland and the presence of concretions forming around the corpora amylacea in the prostatic ducts. (Low power.)

Etiology.—In seeking the cause of prostatic calculi, we must recognize two different etiologic types, namely the endogenous or intraprostatic stones, formed wholly within the gland, and the exogenous or urinary calculi, which reach the prostate from various parts of the urinary tract and become lodged within it. The latter are by far the most frequent and are the type that comes, in the main, for surgical treatment because of the obstructive symptoms they produce.

Endogenous Prostatic Calculi.—These have as their nucleus the minute corpora amylacea, which are physiologic within the prostate. These corpora,

consisting of desquamated epithelial cells and of elements found in the prostatic secretion, such as lecithin and albuminoid substances, have been known since the time of Morgagni (1723) and have also been accurately described by Robin,[51] Virchow,[59] and Albarran.[1] Quite recently the subject has been thoroughly discussed by Moore and Hanzel.[40] Moore found them to be already existent in the fetus at seven months, but to be especially abundant in males over 50 years of age, in whom the tall columnar epithelium of youth, less readily desquamated, has gradually given place to epithelium of low cuboid type, more liable to desquamation, which is further encouraged by the passive hyperemia which overtakes the gland in later years. Senile atrophy of the parenchyma, with partial occlusion of the prostatic ducts and stagnation of their contents, seems also to be a factor in their formation. Whenever, from any cause, these corpora amylacea become increased in size and more abundant in number, they tend to act as foreign bodies, exciting inflammation, whereupon salts of lime become deposited upon them, which in time cause formation of calculi (Fig. 2). Calcium phosphate, calcium carbonate and the organic matter within the corpora unite together to form true calculi. This is especially the case when urine has access to them through a dilated prostatic duct, after which their growth is relatively rapid, and may result in abscess formation and ulceration, as a rule in the direction of the urethra. Such stones, however, may be formed in any part of the prostate gland, and may, under some conditions, remain silent for a long time, giving their owner no trouble whatever until they open into the urethra. While these endogenous prostatic calculi may occur at any age, particularly in individuals suffering from chronic prostatitis, they are more commonly observed in the later years of life, and are as a rule associated with infection or adenomatous hypertrophy of the prostate. In fact, in performing a perineal prostatectomy, in which no diagnosis of prostatic calculi has previously been made, it frequently happens that upon incision of the prostate the knife comes in contact with multiple concretions, calcifications or minute seeds of sand or stones, which may be seen macroscopically.

Exogenous Prostatic Calculi.—These have a different etiology. Coming from the upper urinary tract, from which they may have been expelled by an attack of colic, they arrive at length in the prostatic urethra, where their further progress is blocked by the narrowness of the tract, or by the mechanical obstruction offered by the verumontanum. Such a narrowing may be either physiologic or pathologic. In the latter case it may be the result of an old infection within the prostatic urethra, which has left a permanent contracture, making the passage of any but the smallest stones impossible. Under these conditions, the calculus, developing slowly in its new position, may push back the glandular tissue and form a cavity or diverticulum within the prostate, into which it insinuates itself. Being constantly in communication with the urethra, and hence exposed to the action of urinary salts, such a stone will gradually increase in size as it becomes more and more deeply imbedded within the gland. Now and then one of these calculi, thus ensconced within the

prostate, tends to become further enlarged in a retrograde direction, resulting in a prostato-urethral or even a prostato-urethrovesical calculus. Sometimes a stone may thus become impacted within the prostate without urinary retention occurring, since it may be of too small a size to block the urinary flow, or, again, it may have dug out a channel that permits the urine to flow around it and escape normally, through a perfectly patent urethra.

Among common causes giving rise to small diverticula within the prostate, which invite calculus formation, are traumatism of the prostatic region, bungling attempts at catheterization, and the presence of fistulous openings

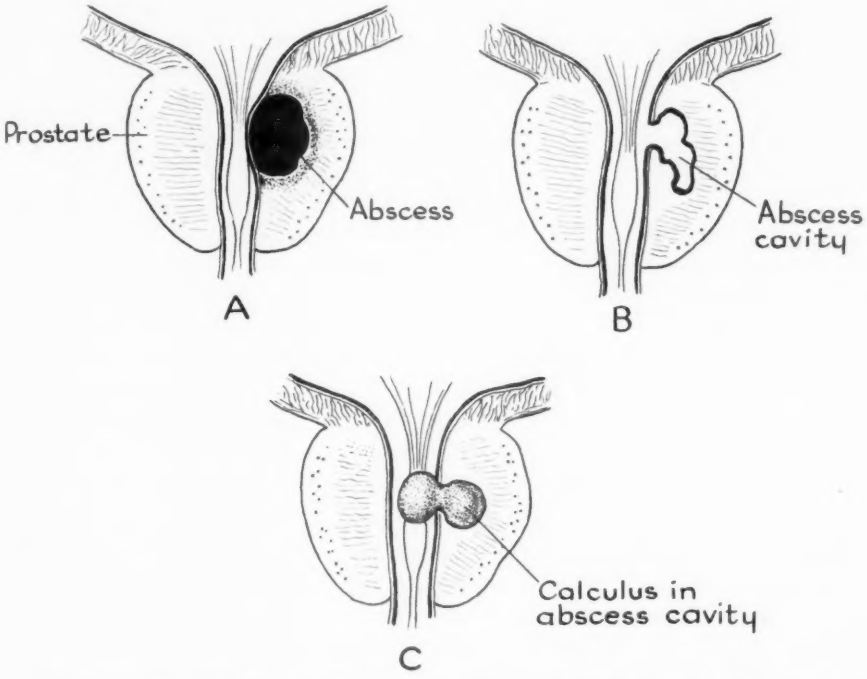

FIG. 3.—Drawing to illustrate the etiology of exogenous prostatic calculi: (A) The prostate with a small prostatic abscess. (B) The cavity of a diverticulum remaining after drainage of the abscess. (C) The prostatic calculus forming within the diverticulum and blocking the lumen of the prostatic urethra.

from prostatic abscesses, the result of long-standing prostatitis (Fig. 3). In addition, the openings of the small glandular orifices or crypts which are the terminations of the prostatic ducts may allow small urinary calculi to become wedged within them, after which such calculi grow like any others exposed to the urinary stream.

All these stones which come from the upper urinary tract while they are still of small size have been termed *migratory*, since they arrive from outside the prostate and take possession secondarily of pockets, diverticula and abscess cavities which have resulted from conditions of infection or traumatism and have ruptured into the prostatic urethra. They then have perfect freedom

either to develop within the prostate or to send branches back into the bladder, building up large calculous masses, sometimes with conspicuous pedicles uniting the prostatic and vesical portions, with the resulting stone resembling a dumbbell or collar-button in its shape. These large stones then become a source of suppuration which may invade large portions of the urinary tract, and may even result in periprostatitis with fistulous openings into the urethra, the rectum, the perineum and even the peritoneal cavity.

Another form of calculus of exogenous type is found in cases in which, after prostatectomy has been performed, a stone develops within the cavity of the remaining capsule of the prostate. Calculi may also be formed after other types of operation, such as external urethrotomies or after operations for drainage of prostatic abscess. Furthermore, we may find instances of *paraprostatic calculi* in which the stone is formed inside a diverticulum of the membranous urethra and closely adherent to the prostate gland, where it has the same surgical significance as the true prostatic calculi (Fig. 1 F).

There is a class of *borderline* cases of endogenous prostatic calculi, in which it is difficult to differentiate, both clinically and anatomopathologically, between endogenous and exogenous calculi. Such a case exists when, because of the racemose structure of the acini of the gland, the multiplicity of the calculi and the large number of ducts opening in the region of the prostatic urethra, a small intraglandular stone finally breaks through the mucosa and opens its way into the lumen of the urethra, constituting what I am inclined to call a mixed endo-exogenous type, because the calculus, although its nucleus originated within the prostate, has beeen brought to the surface of the deep urethra, where it is in contact with the exogenous elements of the urine; these clothe it with layer upon layer of urinary salts, which alter its character, and give it a tendency to grow faster and to become a true prostato-urinary calculus. In some instances several corpora amylacea, or endoprostatic nuclei, have been found combining to form a single stone, covered with exogenous urinary salts. In fact, it is not uncommon to observe in one and the same prostate the two types of calculosis, in which the obstructing symptoms demand surgical relief by removal of the active offending foci.

There is good reason to believe that in addition to the local conditions of lack of drainage, infection, and presence of congenital anomalous pockets in the region of the prostatic urethra, a constitutional factor also plays a part in prostatolithiasis, just as occurs in nephrolithiasis. As a result of this constitutional factor, we may, therefore, observe in the same individual a general urogenital calculosis, expressed in various parts of the urogenital tract (Fig. 1 H).

Pathology.—Whenever a calculus becomes lodged within the prostatic urethra, or within the body of the prostate itself, there will be concomitant infection. Surgical stones are never formed in normal prostates. As a rule, there is a previous history of gonorrhea or some type of urethral discharge which has been present in the patient off and on without his having paid much attention to it. Although in the case of very small intraglandular concretions

the infection may be so slight as to produce no symptoms, nevertheless, routine microscopic examination of the prostatic fluid reveals the presence of many pus cells, indicating that an active focus of infection is present and that the patient is in reality suffering with chronic prostatitis or an infected adenomatous prostatic hypertrophy. In addition many authors have reported the common finding at postmortem of multiple grains of prostatic sand or minute prostatic calculi, visible to the naked eye, in a large percentage of elderly individuals who have died of other diseases.

There is a tendency for this infection to invade the racemose tissue of the prostate and to disseminate through its minute arborizations, resulting in congestion of the organ and appearance of inflammatory attacks within its structure. In time the inflammation produces an abscess of the prostate, with all the symptoms of acute suppurative prostatitis. The abscess may open spontaneously into the urethra, the rectum, or the perineum, but if it fails to evacuate the calculus, a fistula remains and other abscesses may form. Through this fistulous opening urine infiltrates into the recesses of the prostate, causing further complications. A congenital or acquired diverticulum or cyst of the region of the prostate may harbor many hundreds of small faceted prostatic calculi, all sometimes contained in a single pocket. In a study of diverticula of the male urethra, made in 1928, I had occasion to review the literature on the subject, and was able to collect and tabulate 116 cases of this kind. It was interesting to find that in 34 per cent the diverticulum was located in the region of the prostatic urethra, and that in one-half of these cases prostatic calculi were found at the time of perineal operation. When the infection arising from such a collection of stones finds its way into the substance of the gland, extensive abscesses develop with widespread suppuration and breaking down of tissues.

The infection may now pass from the prostate into the entire urinary system, causing the upper urinary tract to react disadvantageously. The bladder is the first organ to feel the brunt of the ascending infection—since prostatic stones are frequently associated with stricture of the prostatic urethra, vesical involvement is a foregone conclusion. The urine becomes cloudy and purulent, and gives off a strong ammoniacal odor. Retention of urine is only a step toward generalization of the infection in the direction of the ureters and kidney pelves. If relief is not obtained by spontaneous evacuation of the calculus, or by operative intervention, a state of general sepsis or a pyelonephritis may result, accompanied by gastric and intestinal disturbances of a grave nature, which in extreme cases may even terminate fatally. More commonly, however, the patient finds relief of symptoms through operation before any such alarming complications set in.

It should always be borne in mind that prostatic stones, like all other calculi, readily act as foci of infection through the blood and lymphatics as well as through the urogenital tract, so that no part of the body is immune from the mischief that they may cause if they remain without proper surgical treatment. At the same time, one should not forget that stones in the prostate,

as a rule, are commonly associated with other pathologic lesions of the urinary tract. In Table I are tabulated the most important lesions associated with prostatolithiasis in this series of cases (Table I).

TABLE I

ASSOCIATED PATHOLOGY IN 29 CASES OF PROSTATIC CALCULI

	No. of Cases
Lesions of the Prostate:	
Calculi with adenomatous prostatic hypertrophy	8
Calculi with chronic prostatitis	7
Calculi with prostatic carcinoma	2
Calculi following prostatic abscess	2
Calculi with calcification in seminal vesicles	1
Stone in diverticulum of the prostatic urethra	1
Calculi with calcifications of Cowper's glands	1
Calculi in prostatic urethra after prostatectomy	2
Calculi in prostate without clinical evidence of other lesions	1
Lesions of the Kidney:	
Nephrolithiasis with prostatolithiasis	2
Horseshoe kidney with prostatic calculi	1
Nephro-ureterolithiasis with prostatic calculi	1
Hydronephrosis with prostatolithiasis	1
Calcifications in hypernephroma with prostatic calculi	1
Calculous pyonephrosis with prostatolithiasis	1
Lesions of the Bladder:	
Carcinoma of bladder with prostatolithiasis	1
Papilloma of bladder with prostatic calculi	1
Prostatic calculi following litholapaxy	1
Vesical stone with prostatic calculi	1
Bladder diverticulum with prostatic calculi	1
Ureterocele with prostatic calculi	1
Bulbous edema in floor of bladder neck	9
Lesions of the Urethra:	
Stricture of urethra with prostatolithiasis	3
Periurethral abscess with prostatic calculi	2
Urethral stone with prostatic calculi	2
Diverticulum of urethra with prostatolithiasis	1
Hypospadias with prostatolithiasis	1
Miscellaneous Lesions:	
Calcifications in adrenal tumor	1
Arthritis	5
Syphilis	2

It is obvious that prostatic stones and their concomitant infection also produce disturbances in the genital function, which cannot be relieved until the stone has been surgically removed. In extreme cases the calcareous deposits within the prostate have a tendency to occupy all the multiple acini in the gland and to destroy the entire parenchyma, resulting in complete calcification of the whole organ (Fig. 4). In some other cases lesions of contiguous organs of the genital tract, such as acute seminal vesiculitis and even bilateral orchiepididymitis, are observed as the result of the infection caused by the prostatic calculi.

Symptomatology.—When the stone is formed primarily within the prostate, from the corpora amylacea, it may cause absolutely no symptoms, and may not interfere in the least with the physiologic functions of the gland. Even exogenous calculi, incarcerated within the prostate by wedging in from the

urethra, may long be silent, since it is not uncommon for the urine to find its way around them if they are not too large, or if they are snugly tucked into a diverticulum within the prostate gland, leaving the urethra patent. In cases of this kind the patient may not have the least suspicion that a stone is present,

FIG. 4.—Drawing from a postmortem specimen of a completely calcified prostate in a patient 61 years of age who had been suffering with *"urethral stricture"* for more than 10 years (after Randall).

and the true state of affairs may be revealed only when a routine physical examination, including urinalysis, brings to light the presence of a few pus cells and red blood cells in the urine—a finding which demands a digital palpation of the prostate gland and roentgenographic studies. Not infrequently the first symptoms from an endogenous stone appear when such a calculus opens into the urethra or is exposed to contact with the urine. As the stone continues to grow in size from infection and gradual deposit of salts, signs of posterior urethritis or chronic prostatitis appear, which cause the patient to consult an urologist.

When an exogenous calculus becomes engaged in the prostatic urethra, the symptomatology is that of an obstructive prostatic hypertrophy. The stone acts as a foreign body and may cause dysuria and vesical contractions as the urethra attempts to expel it and to clear an outlet for the urinary flow. Pain may be moderate, or it may be violent and excruciating, radiating toward the perineum and anus and along the canal of the urethra, or extending to the

abdomen, groins or thighs. In some cases defecation is difficult and painful. Hematuria may appear, chiefly in an initial or terminal form. Sometimes the bleeding may go inside of the bladder, causing blood clots and total hematuria. In a well-established case, where obstructive symptoms have arrived, the pain is constant, varying from a sense of nagging discomfort to the imperative urgency, and burning and frequency such as are experienced in typical cystitis.

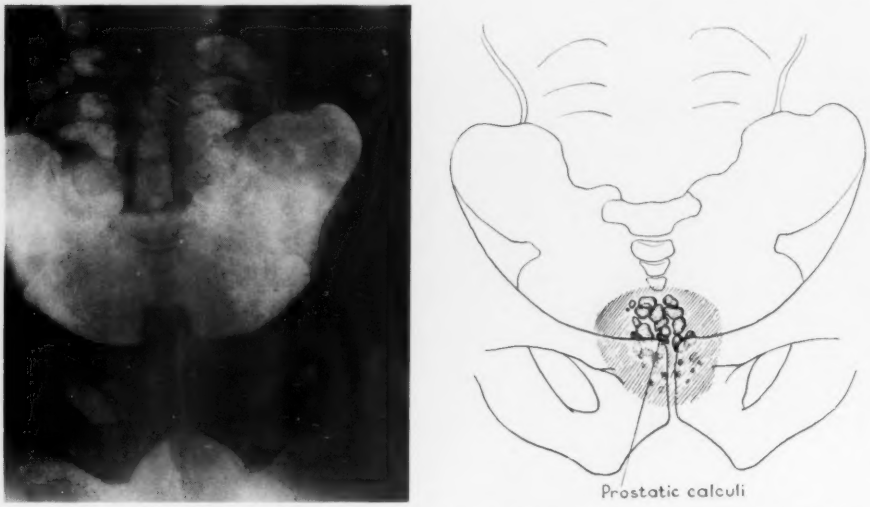

FIG. 5.—Plain roentgenogram revealing the presence of multiple prostatic calculi in Case 29. The accompanying drawing brings out the typical position of the stones in the region of the prostate.

In advanced cases, the general condition will reflect the local distress, and the patient may suffer with all the painful symptoms of an acutely infected prostate and a general toxicity not only of the urinary system but also of the whole body, in some instances manifested in a generalized arthritis. Sometimes the urine contains sand, increasing the difficulty and painfulness of its passage, which may even become impossible. Frequency, dysuria, incontinence, and sudden retention in the midst of urination are all familiar symptoms encountered in cases of prostatic calculi. Stones may be passed, accompanied by the characteristic strangury and colic.

While urinary symptoms are more common than genital, the latter may appear in a certain proportion of cases, in the form of lack of sexual desire, "gleet" or watery urethral discharge and painful and imperfect erections, bloody ejaculation, prickly sensation in the posterior urethra, pain upon ejaculation or impotence. In some cases there is evidence of sterility.

Diagnosis.—The diagnosis of prostatic calculi cannot be made on the basis of the symptoms, since these as a rule show nothing characteristic. In a certain number of cases rectal palpation will give decisive information, and it should be the first recourse if a stone is suspected. Abnormal hardness of the prostate will be suggestive, and it may be that several small, knotty prominences may be felt by the palpating finger. These findings, however,

are still indecisive, until a sensation of fine *crepitation* is elicited, as if stone were rubbing on stone. This sensation is so characteristic and so unmistakable that when it has once been experienced it can never be forgotten—and the diagnosis is plain. When this crepitation occurs, it is indicative of two or

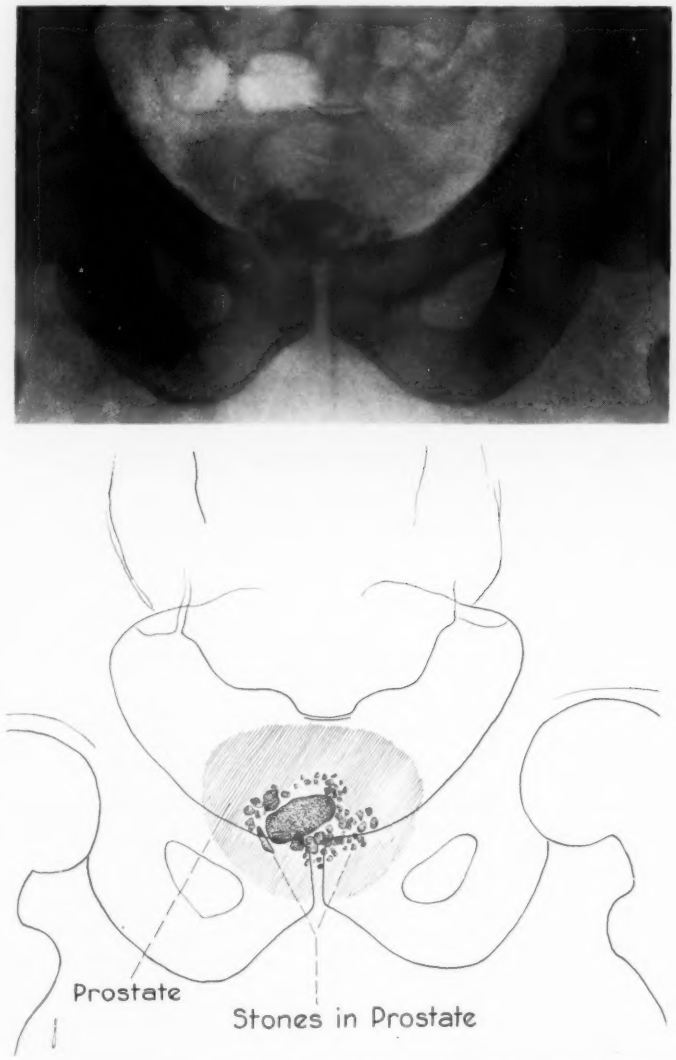

FIG. 6.—Roentgenogram of Case 2: showing the presence of multiple prostatic stones, at the level of the symphysis pubis, in the area of the prostate. The size and position of the calculi are clearly brought out in the drawing.

several small stones within a single pocket within the prostate. It can be obtained from nothing but calculi. If a stone has caused a fistula into the rectum, this too will be recognized by rectal examination. Negative rectal findings, however, will not exclude prostatic calculus.

The location of the stone is of decisive importance for diagnosis. If it is embedded in the middle of the parenchymal portion of the gland it may not be felt upon rectal palpation. However, with a sound placed in the urethra or the cystoscope in position, to make pressure upon the region of the prostatic urethra, and with the finger in the rectum, one may readily feel the calculus, since the tissues in which it lies embedded are thereby made more tense and sensitive as the stone presses upon the urethral sound. In addition, when passing a metal instrument in order to explore the urethra, if the stone is of exogenous type, one can easily hear or feel a click as it scratches upon the metal sound. Although urethral exploration may thus reveal a stone, it is not always clear where it is located, since it may be in the prostate, in Cowper's glands, in a diverticulum of the membranous urethra or in the bladder. Urethroscopy, however, may give a clear view of a small stone or stones projecting through an opening in the region of the prostatic urethra.

Routine cystoscopy and cysto-urethroscopy are also of value because, when the canal is sufficiently patent for the instrument to be passed, they will serve to rule out further pathology in the bladder, such as stone, diverticulum, ureterocele, tumor, *etc.*, and also to visualize accurately the bladder neck, which sometimes gives a typical view of the condition. Moreover, these procedures are of great assistance in determining what type of operation is indicated in each particular case.

The mainstay in the diagnosis, however, is *radiography*. When roentgenograms are properly made they will indicate not only the presence of stones, if such be the case, but also their site, number and size (Fig. 5). In the usual anteroposterior view, if prostatic calculi are in fact present, they will be seen through the shadow of the pubic bone, and protruding above the symphysis pubis, but quite apart from the shadow of the bladder, from which they are separated definitely by a clear space. Even without filling the bladder with an opaque substance, the separation of the prostate from the bladder is clearly recognizable in this position to one familiar with the differentiation (Fig. 6). It is then possible to see whether stones occupy one or both lateral lobes of the prostate; whether they are several or a single stone; and if several, whether these are separate or in groups. Since stone shadows may be superimposed, the exact number of calculi may not be determinable; if the stones are endogenous and small, the image will show a great number of small overlapping shadows in one or two groups separated by a clear space. Another means of differentiation from vesical calculi is given by the size and location; prostatic stones will be in a median position, while a vesical calculus, in order to be median, would have to be of so large a size that it could not be a prostatic stone. In addition to the anteroposterior view, a second film may be made with the rays directed down to the axis of the minor pelvis, in order to avoid the shadow of the pubic bone, which sometimes makes it difficult to visualize small calculi. Shadows of calculi below the symphysis pubis are as a rule stones in a diverticulum of the membranous urethra or Cowper's glands.

Intravenous urograms should be routinely taken, not only to rule out stones

of the upper urinary tract or other pathology of that region, but also to study the topographic relationships of the prostatic calculi in the cystogram. Cystourethrograms should also be made in order to visualize the urethral canal and

FIG. 7.—Roentgenogram illustrating multiple prostatic calculi in a patient 47 years of age, who had been suffering from acute urinary and genital symptoms for several years, and in whom rectal palpation elicited the characteristic crepitation of prostatic calculi. The accompany drawing brings out clearly the position of the calculi. This patient was cured by perineal prostatolithotomy.

to determine accurately not only the position of the prostatic calculus but also to reveal any other concomitant or associated lesions of the region of the prostatic urethra, and, particularly, to rule out prostatic cavities or diverticula, which are so commonly observed.

Differential Diagnosis.—In the differential diagnosis of prostatic calculi, it is important to bear in mind that stone in the prostate may be simultaneously associated with many other clinical conditions from which it must be distinguished. The most common of these clinicopathologic conditions are carcinoma, tuberculosis, chronic prostatitis, adenomatous prostatic hyperplasia, stone or calcification of Cowper's glands, stone of the seminal vesicles, ampulla and vas deferens, or stone in diverticula of the urethra; also multiple minute stones, grains of sand or fine calcareous deposits, casting no shadow in the roentgenogram, and negative to rectal palpation, but discovered during the course of performing a perineal prostatectomy or in sections made in the specimen removed at postmortem. Calcified lymph nodes or phleboliths may also sometimes confuse the roentgenographic picture. Finally, one should not forget that a stone may form in the cavity remaining after prostatectomy, instances of which have been observed in two of my cases.

Since the symptomatology of prostatolithiasis is misleading, no effort should be spared by the urologist and the roentgenologist whenever urographic studies are to be made, *to include the symphysis pubis or area of the prostate in every film.* When he least expects it, the urologist may discover the presence of prostatic calculi which might otherwise never have been diagnosed.

Surgical Management.—Since the treatment of prostatic calculi depends entirely on the merits of the individual case, all types of calculi of the region of the prostatic urethra have been here considered, from the point of view of their surgical treatment. In cases in which prostatolithiasis is an accidental finding in the roentgenogram or in routine physical examination, and in which the patient has no symptoms related to the condition, it is obvious that no treatment is indicated. However, in this silent group of prostatic calculi, which apparently produce no symptoms, a careful urologic examination may reveal that stones are present and that they are, in fact, a source of infection. Evidence of this will be given by the presence of bacteria in the cultures and of many pus cells in the microscopic examination of the prostatic fluid, as well as by the persistent finding of microscopic pyuria and hematuria in the sediment of the urine. I have more than once seen, in the clinics of various New York hospitals, cases in which prostatic and vesical symptoms had received the routine urologic treatment without relief for more than ten years, but in which the underlying conditions appeared to me to be the presence of multiple prostatic calculi, which were, in fact, discovered upon roentgenographic examination. I believe that many cases of so-called recalcitrant or incurable prostatitis which fail to respond to treatment would prove to be cases of endogenous prostatic calculi, if the diagnosis were accurately made by roentgenographic studies.

When the diagnosis is clear-cut, the treatment will depend on the symptomatology, the age of the patient and the type of associated lesions that may be present. The management of the case should be considered from two different points of view—the urologic and the surgical.

In younger patients with minor urinary or genital symptoms, as a rule

associated with chronic prostatitis, the routine medico-urologic treatment of these cases consisting of massage, instillations, irrigations, dilatations, urinary antiseptics, *etc.*, may produce the spontaneous passage of many small stones, although, as a rule, there will be recurrence through persistence of infection and lack of proper drainage. In the event that these patients fail to improve from this routine treatment it appears that the correct indication is perineal prostatolithotomy. But when the calculi are associated with adenomatous prostatic hypertrophy in an older man, the best indication for relief is perineal prostatectomy.

Meanwhile there are many other urologic and surgical procedures that can be applied for special types of cases. For example, if there is a single stone impacted in the area of the prostatic urethra, this can be removed through a cysto-urethroscope, a procedure which I have carried out in two instances. If the stone is impacted in a dilated prostatic duct and is visible through the cystoscope, the duct can be opened by simple fulguration and the stone pushed back with the electrode or with a catheter into the bladder, from which it can then be removed with the cystoscopic rongeur. If there is a median bar or contracture of the vesical orifice, the ideal method of treatment is transurethral prostatic resection, which will serve to remove the obstructing bar and the stones at the same time. A single stone impacted in the utriculus prostaticus can also be removed endoscopically. But when the stones are multiple, disseminated all through the gland and near the capsule, this procedure is contraindicated, for it is certain that by the transurethral route of approach no one will be able to remove all the calculi present within the gland, and the source of infection and the obstructive symptoms will remain. Furthermore, when multiple stones of the exogenous type are impacted in the region of the prostatic urethra, they cause a narrowing of the canal so that the exploring instrument may fail to pass on account of the obstruction they produce; here, therefore, a perineal prostatolithotomy is obviously indicated. In some cases of prostato-urethrovesical calculi, in which most of the stones are of dumbbell or mushroom shape, and in which the greater portion of the stone is within the bladder, the suprapubic route of approach may find its indication. But it appears that most prostatic calculi, as well as prostatic abscesses, are best treated by surgical removal followed by drainage through the perineum. There is less operative shock, less liability to complications, a shorter stay in the hospital and a better convalescence, with results on the whole more satisfactory.

In the historic background of the surgical treatment of prostatic calculi, several avenues of approach have been used: The perineal, through the median line incision, as in external urethrotomy for stricture, urethral stone, *etc.*; the pararectal incision; the hypogastric or suprapubic; the transurethral for litholapaxy, and the rectal avenue. The rectal route was formerly used by a number of continental surgeons, but this has been entirely given up on account of its many complications, such as fistulae and infection, resulting in a high mortality. In view of the marked progress made along the lines of perineal surgery in the last decades by Albarran,[1] Proust,[48] Young,[62] Hin-

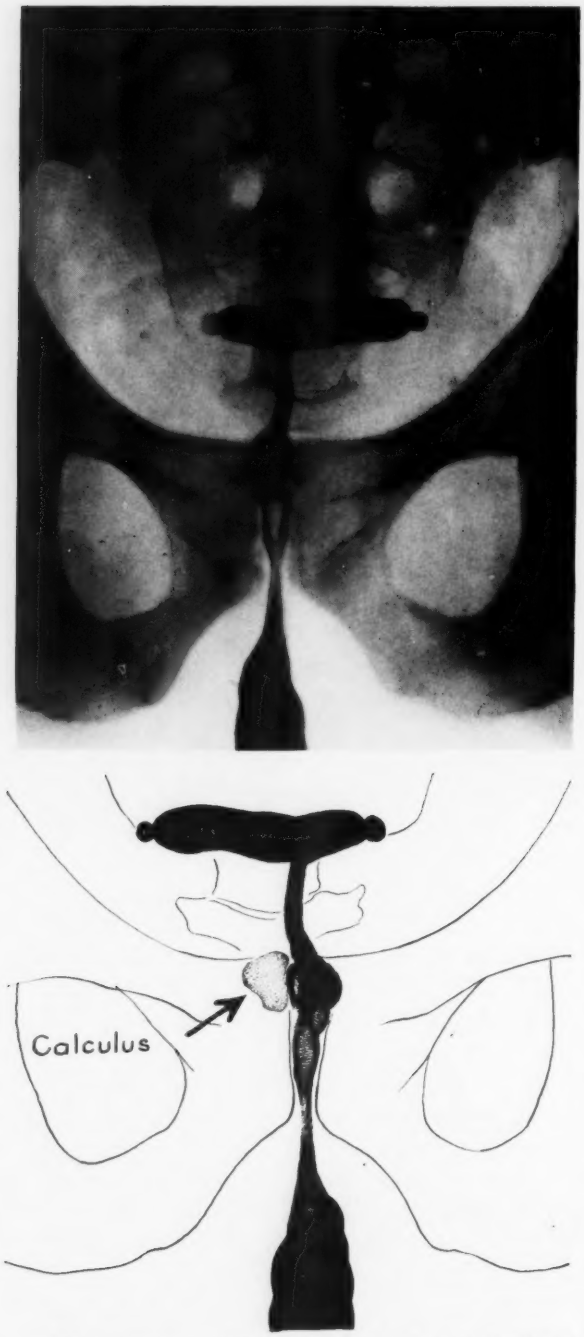

FIG. 8.—Urethrocystogram and drawing of Case 14: Showing a small prostatic diverticulum containing calculi, successfully removed by fulguration and endoscopic manipulation.

man[22] and others, the other routes are now seldom used, so that, as a rule, the perineal operation has become the procedure of choice for the removal of prostatic calculi. Even since transurethral resection has become so popular, the perineal route continues to offer indisputable advantages and is superior in the majority of cases.

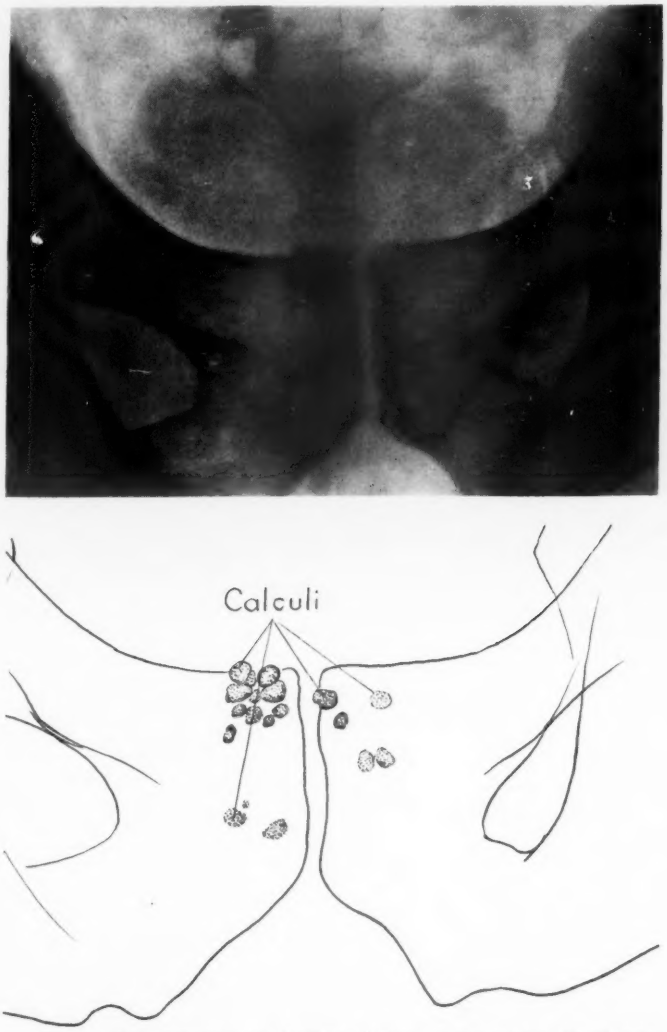

FIG. 9.—Roentgenogram and drawing of Case 20: The patient had suffered from chronic prostatitis and prostatic abscess of long standing. The roentgenogram revealed the presence of multiple prostatic calculi. The patient refused operation and received only conservative medical and urologic treatment.

The open or perineal method secures a complete removal of all the prostatic calculi, many of which would escape detection by the closed or transurethral method, particularly when the calculi are multiple and are associated with prostatitis or adenomatous hypertrophy. It offers a perfect anatomic

exposure, so that the surgeon can follow accurately every step of the entire operation. There are, as a rule, many small stones situated in the plane of cleavage between the adenoma and the prostatic capsule, so deeply situated

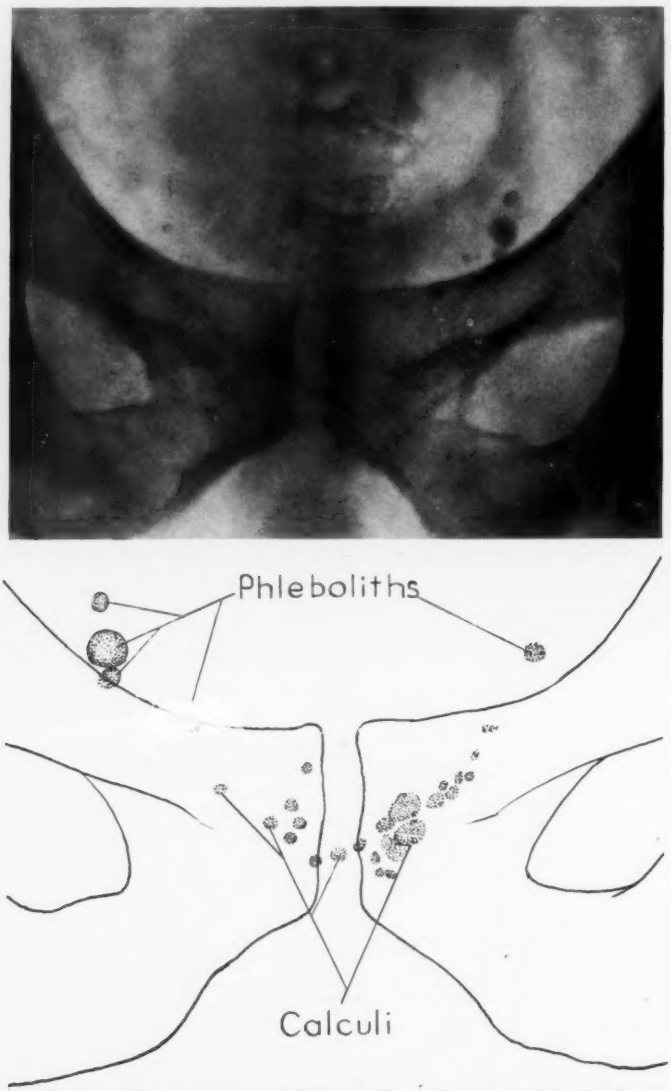

FIG. 10.—Roentgenogram of Case 21: The patient, age 76, had suffered with chronic prostatitis, and had voided small stones on several occasions. Rectal palpation was negative for stones, but the roentgenogram revealed the multiple shadows of calculi in the area of the prostate. The drawing, which has been reversed, indicates the shadows of the calculi and also the presence of phleboliths.

that they cannot be entirely removed either transurethrally or suprapubically. Moreover, in many cases of large-sized stones it is obvious that these cannot be removed from the prostatic bed without considerable trauma, tearing, and

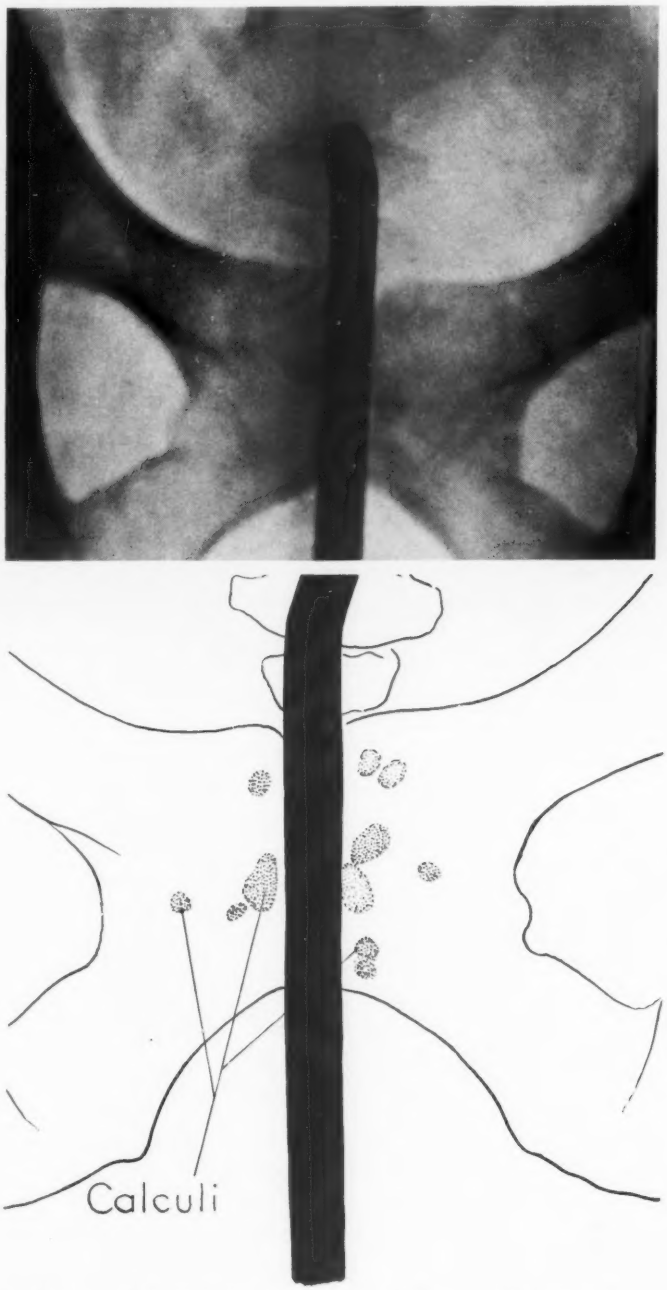

FIG. 11.—Roentgenogram and drawing of Case 6, with cystoscope in place: The patient, age 34, was suffering with acute prostatitis, dysuria and hematuria, in whom the roentgenogram revealed the presence of shadows of small calculi in the area of the prostate. The stones could be plainly felt by rectal palpation.

profuse bleeding, sometimes difficult to control. In addition, it is a well-known fact that most multiple calculi of large size are located in infected pockets, surrounded by a prostatic abscess, and these will be liable to recur and produce sepsis if the cavities are not properly drained to relieve the infection.

Another advantage of the perineal approach is that in certain cases in which stones or calcification exist concomitantly in the ampullae or seminal vesicles, it is possible at the same time to remove these stones through the perineum and provide drainage, as occurs in similar cases of calcification or stones in Cowper's glands or in diverticula of paraprostatic calculi located in the membranous urethra.

In certain cases where a preliminary deviation of the urine by a suprapubic cystostomy is necessary, a two-stage operation may be indicated. Such a case would exist when a traumatic rupture of the membranous or prostatic urethra has left fistulous tracts behind in which prostatic calculi have formed, or when a ruptured prostatic abscess has resulted in perineal or rectal fistulae containing calculi, or in chronic over-distended patients with marked and long-standing suffering from prostatic hypertrophy, in which sepsis, high blood urea, and low renal function demand preliminary drainage and special care in an attempt to have the patient better prepared for the second operation.

Generally speaking, therefore, the ideal surgical procedure for removal of prostatic calculi in well-selected cases appears to be perineal prostatolithotomy, without opening the urinary tract, establishing temporary drainage after operation by merely placing a retention catheter.

Sometimes when the prostatic urethra has to be opened for the removal of the prostatic calculi from the region of the prostatic urethra, there may be two alternatives: one is to drain through the perineum, placing a rubber tube in the bladder as we do in an external urethrotomy or in certain cases of prostatectomy, while the other is to close by interrupted sutures the prostatic capsule and place a self-retaining balloon catheter within the urethra in order to secure good drainage and also to prevent leakage of urine through the perineum.

All these perineal operations on the prostate have been routinely carried out under spinal anesthesia.

Technic of Perineal Prostatolithotomy.—The technic for the perineal exposure of the prostate is essentially the same that has been described elsewhere[18] in the report of more than 200 perineal operations for removal of the prostate and seminal vesicles. After the prostate has been surgically exposed the technic varies from that previously described only in the making of a curved transverse incision upon the surface of the prostate instead of a vertical one, in order to open the prostatic capsule and remove the stones without opening the membranous urethra. This secures a better exposure and allows complete removal of all the calculi, after which, if there is no pus, the capsule is closed with chromic catgut without drainage, placing a retention catheter through the urethra for three or four days in order to put this canal

at rest and secure drainage from the bladder. However, when there is a small pocket of pus present a cigaret drain should be left in one angle of the wound. When the calculi are multiple and are located in the region of the prostatic urethra, it may be necessary to open the latter during the prostatotomy operation. If there is considerable pus, however, it will be better to drain it

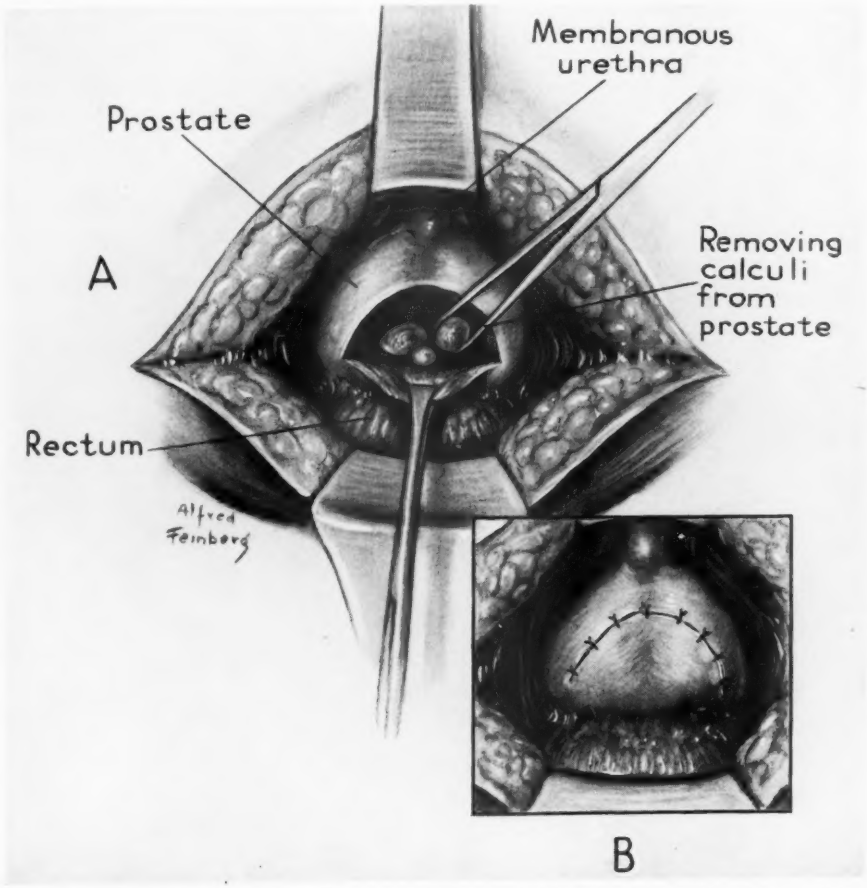

FIG. 12.—Operative technic of perineal prostatolithotomy: (A) The perineal surgical exposure of the prostate, showing a transverse incision on the surface of the gland for the purpose of removing all the calculi that may be present. (B) Method of closure of capsule by interrupted sutures.

perineally by introducing a good-sized catheter through the perineum into the bladder. But if the operation is aseptic and there is a clear-cut exposure of the whole anatomic region, the capsule of the prostate is closed in the usual manner, leaving a cigaret drain in one angle of the perineal wound, and inserting a self-retaining balloon urethral catheter through the urethra into the bladder to serve as an hemostat and to secure perfect drainage, thus facilitating the prompt healing of the wound. As a rule, the cigaret drain is removed 24 to 48 hours after the operation, the retention catheter on the fourth or fifth day, and the stitches on the sixth or seventh day. The patient is al-

lowed to sit out of bed at this time, and to leave the hospital after 12 to 14 days, in the average case, with the perineal wound completly healed.

Perineal Prostatectomy for Removal of Prostatic Calculi.—The common occurrence of prostatolithiasis in association with adenomatous hypertrophy has been clearly recognized in these modern days of accurate urologic investigation. While the main feature of the condition is the obstructive pathology caused by the enlargement of the gland, producing all the urinary symptoms of

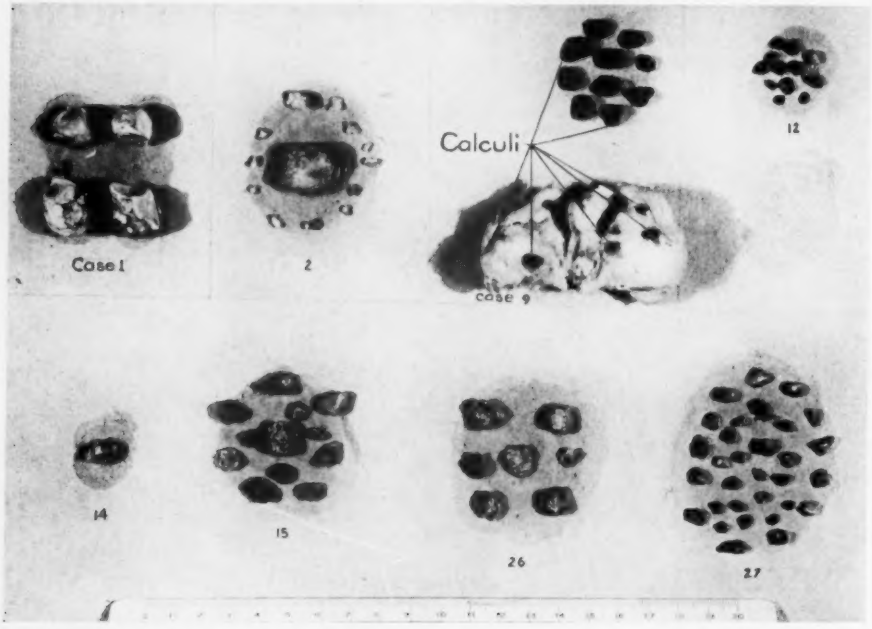

FIG. 13.—Photograph of a collection of prostatic calculi (actual size) removed by the author. The two lateral lobes of the adenomatous prostate removed from Case 9 are shown with multiple calculi impacted within them. Observe, above the organ, another group of prostatic calculi removed from the same case.

prostatism, the multiple, minute, seed-like stones or grains of sand frequently present in the gland are sometimes not revealed until a perineal operation brings them to view. Two groups of cases must, therefore, be kept in mind: one, in which the stone is diagnosed before operation by rectal palpation or by roentgenographic examination of the gland, and the other, in which rectal palpation reveals no concretions or may barely suggest the concomitance of very minute grains of sand, but in which roentgenographic examination shows no evidence of stone shadows because the concretions are composed chiefly of organic substances, which are not opaque to the roentgen ray.

These two groups of prostatolithiasis cases, which are commonly associated with hypertrophy of the gland, come to the urologist for relief of urinary symptoms caused, as a rule, not by the stones but by the obstructive adenomatous pathology. Upon careful urologic examination evidence is found of an infected adenoma, sometimes associated with prostatitis and seminal vesiculitis. This is so much the case that one is accustomed to observe the notable shrink-

age of the gland after cystostomy has been performed as the preliminary drainage in preparation for prostatectomy.

It appears that these two conditions are better handled by an open surgical procedure, in order to remove the entire mass of adenomatous tissue and at the same time the multiple calculi accompanying it. The calculi may be found anywhere within the gland, but as a rule they are most commonly met with beneath the submucosa of the prostatic ducts where these open into the urethra

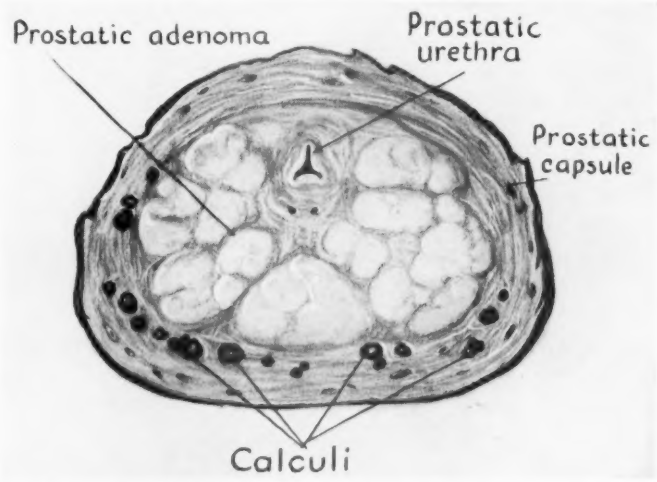

FIG. 14.—Drawing of a cross-section of an adenomatous prostate removed by the perineal route from Case 23: Observe the characteristic location of the prostatic calculi in the plane of cleavage between the adenoma and the capsule, indicating the great advantage of a total perineal prostatectomy over the method of transurethral resection. It is obvious that most of the calculi are situated beyond the reach of the resectoscope.

or in the plane of cleavage of the adenoma, almost in contact with the capsule of the gland, thus demonstrating the superiority of the perineal approach in this type of case (Fig. 14).

Technic of Perineal Prostatectomy for Prostatolithiasis.—In the perineal approach to the prostate, the technic of the first step of the operation is the same as that for perineal prostatolithotomy, except that the transverse curved incision on the posterior aspect of the capsule of the gland is carried deeper in the center, in order to open the floor of the prostatic urethra through which the prostatic retractor is introduced into the bladder. The purpose of the insertion of the retractor is to hold the gland firmly in position and give better exposure. Its complete enucleation can be carried out without opening the membranous urethra. The enucleation is then accomplished by entering the plane of cleavage between the capsule and the adenomatous tissue, which can be easily done by blunt dissection with the index finger; loosening the gland from its attachment and from the floor of the bladder neck, so that the whole specimen of the prostate can be removed in one piece (Fig. 15). During this manipulation many small prostatic calculi can be seen on the surface of the adenomatous gland. After complete hemostasis has been obtained, the bladder

neck is sutured to the membranous urethra, placing a self-retaining balloon catheter in the urethral canal. The edges of the capsule of the prostate are brought together by interrupted sutures, leaving a cigaret drain in the space of the prostatic bed, after which the wound is closed by bringing together the two levator ani muscles as in any other perineal operation. The results from

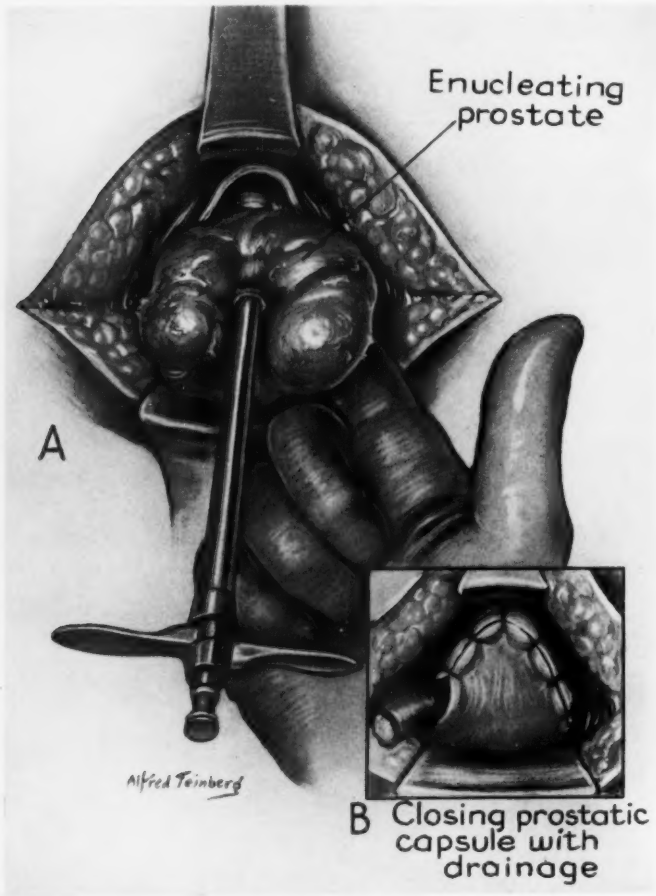

FIG. 15.—Drawing to illustrate the operative technic of perineal prostatectomy, particularly when prostatolithiasis is associated with adenomatous hypertrophy. (A) After the usual perineal surgical exposure, the capsule is opened and a retractor inserted through the prostatic urethra into the bladder, without opening the membranous urethra. The nucleation of the adenoma is then accomplished with the index finger, following the line of cleavage, thus removing the entire organ in one piece. (B) The capsule is closed by interrupted sutures, leaving a cigaret drain in one angle of the wound. (See text.)

use of this technic have been very satisfactory. The cigaret drain, or gauze packing, is removed on the second or third day, the sutures on the sixth day, and the retention catheter after about a week or ten days. With this thoroughly anatomic surgical procedure, a complete removal of the entire adenoma and all the prostatic calculi can be accomplished, effecting permanent cure.

Other Surgical Procedures in Cases of Prostatolithiasis—Associated with

Other Lesions of the Genito-urinary Tract.—It is a common finding that in the presence of prostatolithiasis there may be coexistence of other calculosis elsewhere in the urinary or genital tract, which may demand surgical relief. In other words, prostatic calculus does not exclude calculus in the kidney, ureter, bladder or even in the genital or lower urinary tract; on the contrary, a generalized uroprostatolithiasis is to be expected (Table 1). Cases of this kind should be handled according to the type of pathology they present. In each individual case it must be determined which lesion is the most important and which should, accordingly, be attacked first. In some cases of combined prostatolithiasis and nephrolithiasis, the best clinical results can be obtained by first removing a functionless pyonephrolithiasic kidney, or the stones that are producing pus and destruction in a kidney pelvis, deferring until later the removal of the prostatic calculi, since it is obvious that the pus coming from the upper urinary tract is bound to contaminate the operation upon the lower tract. In certain cases of prostatolithiasis associated with calcifications, concretions or calculi in the seminal vesicles, in which there is evidence of vesicular infection, it may be desirable to perform a combined prostatolithotomy and vesiculolithotomy; in some instances, it may even be wise to carry out a combined and more radical procedure of perineal prostatectomy with seminal vesiculectomy.

Prostatolithiasis Associated with Carcinoma.—The borderline diagnosis of an indurated nodule palpated in the surface of the prostate always suggests the association of malignancy with lithiasis. It must be kept in mind that these two lesions are not infrequently observed together, in which case the differential diagnosis can be accurately made roentgenologically and by a needle biopsy. If there is no evidence of metastasis, or that the malignancy has expanded beyond the capsule, a total radical perineal prostatectomy appears to be the procedure of choice, but when general bony metastasis or carcinosis is obviously present, in association with the stones or calcification in the prostate, it appears that the best treatment is the removal of the obstructing lesion from the vesical orifice by transurethral resection for the purpose of at least relieving the agonizing urinary obstructing symptoms and securing better drainage, while the carcinoma continues its inevitable progress.

Recurrence of Calculi after Prostatectomy.—When the exogenous type of calculus forms again in the prostatic urethra or in the space left behind after suprapubic or perineal prostatectomy, the surgeon must exercise judgment in the choice of the route to be followed. When the stone lodges in the prostatic bed and there is not much infection in the bladder, it can sometimes be removed through cystoscopic manipulations or by simple cystoscopic litholapaxy. In other cases it may be preferable to remove the stone suprapubically. This removal can of course also be carried out by way of the perineum, but it is often much safer to use the suprapubic route for the removal of these large stones, which in most instances extend into the bladder, causing retention and back pressure. Corlineau,[9] in 1932, collected 103 cases of this type from the literature, indicating that the recurrence of calculi is not uncommon following prostatectomy.

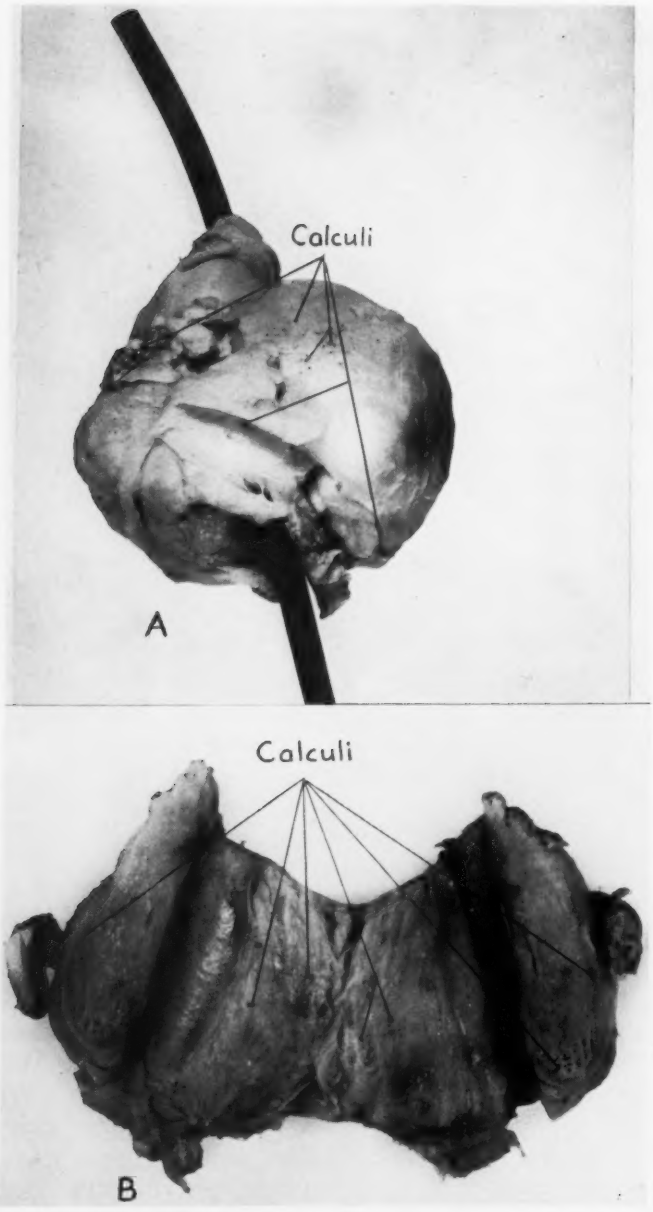

FIG. 16.—Photograph of an enormous adenomatous prostate removed from Case 5, by perineal prostatectomy. (A) The specimen, removed in one piece at operation, is seen mounted on a catheter, and shows multiple minute calculi scattered over the surface of the organ. (B) The same specimen split open, showing the trilobar adenomatous hypertrophy and the presence of innumerable seed-like prostatic calculi, which were an accidental finding at operation.

ILLUSTRATIVE CASE REPORTS

Case 1.—*Perineal prostatotomy for the removal of prostatic calculi:* A. T. E., age 47. Married 15 years. No children. Chief complaint: Frequency, burning, difficult urination, and pain in the perineum for several years. The patient had consulted another physician who had massaged his prostate, given him hot rectal douches and instillations for three years without relief. On September 27, 1934, he consulted my associate, Dr. James Pedersen. Rectal examination disclosed that he was suffering from prostatic calculi. The crepitation of the stones could be felt and almost heard by rectal palpation of the gland. An attempt to explore the urethra and pass a catheter failed, possibly owing to the obstruction caused by one of the stones implanted in the prostate and occupying the lumen of the canal. The voided specimen of urine was cloudy with moderate amount of sediment, containing a heavy amount of albumin, many red blood cells and innumerable pus cells with large clumps.

Operation.—Under spinal anesthesia, with the patient in exaggerated lithotomy position, an attempt to pass a sound through the urethra failed, since one of the stones was blocking the channel of the prostatic urethra. Without instrumental guidance, therefore, a semilunar incision was made in the perineum between the two ischial tuberosities. The central tendon was cut and with further dissection the recto-urethralis muscle was divided and the bulb of the urethra retracted from its attachments. With two lateral retractors the two levator ani muscles were separated, and by further dissection the membranous urethra was exposed at the apex of the prostate. A sound was then passed through the meatus of the urethra so as to allow the passage of the urethral retractor, in order to hold the prostate in position. The layers of Denonvilliers' fascia were incised and stripped back and the posterior surface of the prostatic gland readily exposed. Two vertical incisions were made in the prostate, leaving a bridge of tissue in the middle for the protection of the urethra with its verumontanum and ejaculatory ducts. The index finger was inserted into each side of the prostate and by further manipulation four stones, each about the size of an olive, were removed from the prostate gland. Very little bleeding was encountered. Cigaret drains were placed on both sides of the prostate, and two sutures were placed in each side of the prostatic capsule. The wound was then closed in the usual manner, urethral retractor removed and a soft rubber catheter No. 18 F. was passed into the bladder through the urethra and left in place for drainage. The operation was completed by approximating the two levator ani muscles of the perineum, and closing the floor of the pelvis by a double chromic catgut suture. Interrupted silkworm gut sutures to skin incision.

Postoperative Course.—The patient made an uneventful recovery, and left the hospital with perineal wound nearly healed, 13 days after operation. His general condition gradually improved, and he is free from symptoms at the present time.

COMMENT.—This case illustrates the importance of properly recognizing the multiple prostatic calculi and the good results obtained by an open operation.

Case 2.—*Perineal prostatolithotomy for the removal of multiple prostatic calculi in a case of longstanding so-called incurable urethritis and prostatitis with stricture of the urethra:* R. F. D., age 45. Examined January 14, 1934. The patient stated that he had passed stones since the age of eight, with attacks of chills and fever. Occasional hematuria, pyuria, pain often severe, in right lumbar region and perineum, and in addition generalized rheumatic pains. Married 17 years, no children. No sexual desire and complains of sterility. Had been hospitalized elsewhere on two other occasions. Voided specimen of urine is cloudy and loaded with pus. Rectal examination revealed an enlarged prostate, boggy in consistency, and filled with calculi. Seminal vesicles indefinitely palpable. Miscroscopic examination of prostatic fluid showed more than 100 pus cells per field, with clumps. Both kidneys tender and palpable. External genitals negative, except

that right epididymis was nodular. Exploration of urethra difficult. Residual urine 16 cc. Roentgenologic examination, January 16, 1934, revealed minute, multiple shadows in the area of the prostate and a larger one about the size of an olive in the center. The patient was treated for a while with gentle prostatic massages, sound, bladder irrigations, Kollman dilatation, without complete relief. There was a definite stricture of the urethra, so that catheter No. 18 F. passed with great difficulty; but gradually the canal was dilated to pass No. 24 F. Kollman dilator was also stretched to 29. During these manipulations the patient bled and apparently passed small fragments of calculi. Cystoscopy revealed that the interior of the bladder was normal, but examination of the prostatic urethra showed two definite holes or openings of diverticula in either side and in the middle portion of the prostatic urethra. These prostatic orifices were about the size of a pea and when probed with a bougie appeared to be half an inch deep. The verumontanum appeared to be smaller than normal, but no stone or tumor mass was seen in the lumen of the urethra. It was concluded, therefore, that the prostatic calculi were definitely intraprostatic. The possibility of transurethral prostatic resection was at first considered, but it was decided that there were too many calculi present, disseminated through the gland, many of them almost in contact with the capsule. There was also some fluctuation in the gland on rectal palpation which suggested the concomitance of prostatic abscess with prostatolithiasis. Perineal prostatolithotomy was, therefore, undertaken. This procedure was successfully carried out February 24, 1934, at the Murray Hill Hospital, using the same operative technic as in the previous case, except that a transverse curved incision was made on the prostate, which gave a better surgical exposure for the removal of all the prostatic calculi.

Case 3.—*Small intraprostatic calculi, with no operation:* F. M., age 54. Referred, October 11, 1935, for prostatic treatment. He had slight frequency day and night and sometimes dysuria and a dull pain in perineum. Has been having treatment off and on for prostatitis. Voided specimen of urine clear with shreds. Rectal examination revealed an enlarged prostate three and one-half times its usual size, and of leathery consistency. Between the left side of the midline and the posterior lobe a nodule could be felt, about the size of an olive pit, suggesting the possibility of prostatic calculi. The surrounding tissue was slightly fluctuating, giving the impression that the stone was inside of a small pocket in the posterior lobe of the intraparenchymal portion of the gland. The microscopic examination of the prostatic fluid revealed 20 pus cells per field. Patient has 90 cc. residual urine. *Clinical Diagnosis:* Chronic prostatitis and prostatic calculi.

October 25, 1935: Cystoscopy revealed a slight degree of median lobe prostatic hypertrophy, also slight hypertrophy of the trigone and interureteric ridge, marked bullous edema of the area of the prostatic urethra and vesical orifice, probably due to the presence of prostatic calculi. Roentgenographic studies revealed on either side of the cystoscope a group of small round shadows, suggesting the presence of multiple prostatic calculi. The pyelographic studies showed an associated lesion of right nephroptosis with hydronephrosis. Perineal prostatotomy was advised for removal of the calculi, but patient preferred to have conservative medical treatment. He was, however, cystoscoped and endoscoped on several occasions. The stones in the prostate, felt by rectum, were not seen through the cystoscope, and it was believed that they were situated deep in a lobe of the prostate close to the capsule, where they were without communication with the lumen of the urethra. However, on December 8, 1936, a urethroprostatocystogram was taken which revealed a small diverticulum, possibly a dilated prostatic duct, which appeared to have a connection with some of the prostatic calculi seen in other pictures. As the patient persisted in his refusal to be operated upon, the calculi are still present in the prostate, and he is now suffering from acute arthritis of the right shoulder.

COMMENT.—This case illustrates the persistence of infection harbored in a prostate containing calculi and the complications that may arise from not hav-

ing had an open operation to remove the stones which constitute the focus of infection, from which the arthritis in this patient originated.

Case 4.—*Two-stage perineal prostatectomy in a greatly debilitated patient in whom adenomatous prostatic hypertrophy was associated with complete retention and cardiorenal dysfunction. Prostatic calculi found at operation:* J. C. C., age 63. Examined May 11, 1931. The patient complained of pain across the back and frequency of urination day and night. Has been having treatment for a cardiac lesion. Had gonorrhea 30 years ago, and has suffered, for 20 years, with difficulty of urination. Has recently had two attacks of total hematuria, with innumerable blood clots removed from the bladder. Rectal examination revealed an enlarged, leathery prostate of the adenomatous type. Cystoscoped May 14, 1931: Interior of bladder negative except for evidence of hypertrophy of the median and two lateral lobes. There were also two small cysts on the roof of the vesical orifice with some bullous edema of the floor. After a few days of preliminary catheter drainage, a cystostomy was performed, under local anesthesia. Three weeks later, when the blood chemistry and P.S.P. test were within normal limits, a perineal prostatectomy was carried out in the usual manner, under spinal anesthesia. The prostate removed was of considerable size, and when the capsule was incised it was noticed that multiple small grains of sand or seed-like calculi were present. Patient had an uneventful convalescence and left hospital, three weeks after operation.

COMMENT.—This case illustrates the advantage of a two-stage perineal prostatectomy as a safe procedure in advanced cases of adenomatous prostatic hypertrophy of long standing, when the patient's general condition is so impaired that it demands preliminary preparation to restore cardiorenal function. Cases of this type complicated with prostatic calculi demand suitable drainage preliminary to prostatectomy. Multiple prostatic calculi accidentally found can be removed more easily and more completely by the perineal route than in any other way, since the innumerable minute stones found in the line of cleavage between the adenoma and the prostatic capsule can not be reached properly by any other method of approach.

Case 5.—*Case of silent prostatic calculi, found at operation, in an enormous adenomatous prostate:* A. G. M., age 62. Examined May 15, 1936. The patient was suffering with an attack of complete retention of urine. The retention was relieved by catheter and the distended bladder was found to contain 22 ounces of clear urine. He stated that he had had other attacks of retention on two or three earlier occasions and had been relieved by a soft rubber catheter. He also complained of difficulty and frequency of urination, pain in perineum, chronic constipation and sometimes pain in the suprapubic region. Rectal examination revealed a greatly enlarged adenomatous prostate. A total perineal prostatectomy at the Murray Hill Hospital, under spinal anesthesia. Although the preoperative diagnosis of prostatic calculi was not made and no roentgenograms were taken in this case, multiple stones were readily seen, at the time of the perineal operation, when the prostatic capsule was opened (Fig. 16). This case belongs in that group in which the preoperative diagnosis of prostatic calculi is not made until during or after the operation. The prostatectomy was carried out for the obstructing pathology caused by the enlargement of the prostate. The operative technic employed was as follows:

Total Perineal Prostatectomy.—After the usual preparation, with the patient in the exaggerated lithotomy position, a No. 26 F. sound was passed into the bladder without difficulty. A curved incision was then made in the perineum, running from one ischial tuberosity to the other, at about the level of the medial portion of the perineum. The incision cutting the skin and superficial fascia was deeper at each side of the middle line. Then with the handle of the knife the two ischial fossae were well separated by blunt

dissection. A bifid perineal retractor was placed in position, retracting the lower lip of the perineum and central tendon and recto-urethralis muscle were cut through; the two levator ani muscles were separated and retracted. The remaining fibers of the recto-urethralis muscle were cut with scissors; the bulb was separated from its attachment to the apex of the prostate with a bulb retractor. Denonvilliers' aponeurosis was exposed by blunt dissection. The bifid perineal retractor was then replaced by a perineal retractor. With a good exposure, a transverse curved incision was made on the surface of the prostate, opening the prostatic urethra about one-half inch from the membranous urethra, which, although exposed, was not disturbed, in order to protect the external sphincter. The sound, used as a guide and properly placed in the urethra, was then removed and, while the prostatic urethra was open in its middle portion and held with two pairs of Allis' clamps, Young's prostatic retractor was inserted into the bladder through the prostatic urethra without difficulty. The adenomatous prostate then came readily into view and enucleation with the handle of the knife was begun; inserting the index finger inside of the capsule and all the way around the prostate, which was found to be rather easy, a total, intracapsular prostatectomy was carried out without difficulty. Very little bleeding was encountered; two sutures were placed in each side of the prostatic capsule in an attempt to close this cavity, also to bring the portion of the membranous urethra tightly up to the neck of the bladder and floor of the prostatic bed. A small packing was placed inside of this prostatic space. The wound was closed in the usual manner, beginning with the two levator ani muscles, which were drawn together with double chromatic catgut sutures which closed the floor of the perineum tightly. The skin was closed with interrupted silkworm gut sutures, leaving the packings of gauze fastened to one side of the perineum. A soft, No. 22 F., rubber catheter was passed through the urethra and placed in position for permanent drainage.

COMMENT.—This case illustrates the silent type of multiple minute prostatic calculi accidentally discovered in a case of perineal prostatectomy for adenomatous prostatic hypertrophy. The association of prostatolithiasis and adenomatous hyperplasia, while not suspected preoperatively, is in fact quite a common observation.

Case 15.—*Perineal prostatolithotomy for drainage of prostatic abscess and removal of prostatic calculi:* J. N. S., age 68, complained of frequency, burning, dysuria, bladder tenesmus, and pain in the rectum and perineum. He had had a previous operation for rectal fistula 30 years ago. Rectal examination disclosed an enlarged adenomatous prostate of leathery consistency. There was a definite area of fluctuation in the right lateral lobe. Small nodules of prostatic calculi could be felt by rectal palpation. Cystoscopy revealed bullous edema of floor of bladder neck. Roentgenograms disclosed multiple shadows of calculi in area of prostate. A perineal prostatotomy was performed under spinal anesthesia. When the prostate was exposed, by the usual perineal technic, some induration and fluctuation was noticed on the surface of the gland. A transverse incision was made in the capsule of the prostate and considerable pus evacuated. At the same time, a few prostatic calculi were removed. The prostatic cavity was curetted and packed with iodoform gauze. The patient had an uneventful convalescence and left the hospital three weeks after operation.

COMMENT.—This case illustrates the association of prostatic calculi with the formation of prostatic abscess—which demands the removal of the calculi. It also shows the advantage of perineal surgical drainage in order to obtain a permanent cure.

Case 23.—*Association of prostatic calculi and carcinoma of the prostate:* M. G., age 64, had been suffering with frequency, dysuria, and difficulty in urinating for several

years. There was a history of G.C. on three different occasions. Rectal examination disclosed the prostate to be enlarged, and stony hard in consistency, suggesting carcinoma, and the possibility of small, seed-like prostatic calculi. A hard nodule was felt in the posterior lobe. The seminal vesicles were distended and chronically inflamed. There were six ounces of residual cloudy urine. Cystoscopic examination revealed congestion and swelling of bladder neck with marked bullous edema and distortion of the prostatic urethra. After the preliminary preparation, patient had perineal prostatectomy performed for removal of an adenocarcinoma, in which calcifications and multiple calculi were found. Patient had a fairly good recovery although he had a perineal fistula, which, after dilatation of the urethra, healed entirely. He was discharged in good condition.

COMMENT.—This case illustrates the association of carcinoma of the prostate with the presence of prostatic calculi. It is a type of case which is sometimes difficult to differentiate clinically, but by roentgenography, needle biopsy, and histologic examination of the specimen removed at operation, the diagnosis can be accurately made, as was done in this case.

Case 26.—*Prostatolithiasis associated with nephrolithiasis:* L. C., age 48, complained of a lumbar fistula which had persisted for six months following a nephrolithotomy. He also suffered with frequency, dysuria, pyuria, burning and difficulty in urination. The patient had been operated upon elsewhere for the removal of a stone from the left kidney. Roentgenograms revealed some shadows in the area of left kidney indicative of stone, which may be the cause of the infection and the reason why the lumbar wound refused to heal. Complete work-up shows the left kidney to be functionless and the right kidney to have a good urea and P.S.P. output. Pyelograms also reveal complete destruction of the left kidney, with associated evidence of calculi in the area of the prostate. A left nephrectomy was performed, followed one year later by a perineal prostatolithotomy for the removal of the prostatic calculi. The patient is, at present, well and free from urinary symptoms.

COMMENT.—This case illustrates the advantage of a complete urologic examination in order to establish an accurate preoperative diagnosis. It also shows the wisdom of first removing the nephrolithiasic, functionless kidney, and attacking the prostatolithiasic problem at a later date, in order to obtain a permanent cure.

SUMMARY OF 29 CASES OF PROSTATIC CALCULI

In this series of cases, all the patients were suffering with urinary symptoms, ranging from simple frequency and dysuria to hematuria, tenesmus and complete retention of urine. Genital and rectal symptoms were also quite frequently observed. Most of the patients, however, came to the urologist complaining of a combination of urinary, genital and rectal disturbances.

In some of these cases, the prostatolithiasis was associated with other pathologic conditions within the urinary tract, as noted in Table I. In some instances, in fact, there was evidence of a generalized lithiasic condition affecting various organs of the genito-urinary tract, demanding a complete urologic examination and appropriate surgical treatment.

A summary of the 29 cases is presented in Table II. Here, it can be seen that in some cases it has been necessary to first perform an operation for removal of a functionless nephrolithiasic kidney (Case 26), and then, at a latter

TABLE II

SYNOPSIS OF 29 CASES OF PROSTATIC CALCULI

Case No. Name	Date of Exam.	Age	Symptoms	Clinical Findings	Roentgenologic Diagnosis	Treatment Urologic	Treatment Surgical	Results
1 A. T. E.	10-16-34	47	Frequency, burning, difficulty, pain in perineum. Painful erection. Sterility. Arthritis	Rectal examination elicited crepitation of prostatic calculi. Pus and bloody urine; 100 pus cells in prostatic fluid per H.P.F.	Multiple prostatic calculi	Prostatic massage. Bladder lavage. Hot rectal douches	Perineal prostatolithotomy	Cured
2 R. F. D.	1-16-34	45	Hematuria, pyuria, pain in perineum, generalized arthritis. Painful erections, and ejaculations. History of sterility. Passing stones since the age of eight	Prostate full of stones; marked crepitation. 100 pus cells in prostatic fluid per H.P.F. Stricture of urethra	Shadows of multiple calculi in the area of the prostate	Prostatic massage; sounds; bladder lavage; deep instillations	Perineal prostatolithotomy	Cured
3 F. M.	10-11-35	54	Frequency day and night, dysuria, dullness in perineum and rectum. Anemia. Rheumatoid arthritis	Urine clear, with shreds. Enlarged prostate with calculi in intraprostatic portion of posterior lobe. 20 pus cells per H.P.F.	Small prostatic calculi with associated right nephroptosis and hydronephrosis	Cystoscopy with dilatation of ureters and kidney pelvis lavage. Prostatic massage; deep instillations; sounds, *etc.*	Refused operation	Still suffering from arthritis and minor urinary symptoms
4 E. J. C.	5-11-31	63	Pain across back. Frequency, nocturia, difficulty, pain in perineum and on defecation. Recently had two attacks of hematuria and has a cardiac condition	Rectal examination disclosed adenomatous prostatic hypertrophy	No shadow of stone. Minute calculi found at time of operation	Cystoscopy. Bladder lavage. Indwelling catheter	Two-stage perineal prostatectomy. Recurrence of of stone; removed by cystoscopic litholapaxy	Recurrence of symptoms, with stone in prostatic urethra two years later. Cured after second operation
5 A. E. M.	5-15-36	62	Complete retention of urine. Has had two or three previous attacks. Difficulty, frequency, day and night. Pain in rectum and bladder region	Retention 22 oz. Bladder distended to umbilicus. Adenomatous prostatic hypertrophy. Stone not felt	Calculi found at operation	Retention catheter inserted	Total perineal prostatectomy for removal of adenomatous prostatic hypertrophy; with calculi found at operation	Cured

6 A. B.	10- 8-35	34	Hematuria, marked frequency day and night, dysuria, pyuria, pain in perineum. At times chills and fever. Acute prostatitis and urethritis.	Enlarged and chronically inflamed prostate full of stones. Residual urine 2 oz.	Multiple shadows of prostatic calculi	Cystoscopy. Intravenous urograms. Urethrocystogram	Refused operation	Advised prostatolithotomy. Patient never came back
7 E. C.	4- 6-34	34	Several types of gonorrhea with persistent urethral discharge. Stricture of the urethra. Dysuria, dribbling, Wass. 4†	Enlarged prostate chronically inflamed. 20 pus cells per H.P.F. in prostatic fluid. Positive cultures. Evidence of chronic prostatitis and seminal vesiculitis	Small shadows of prostatic calculi. Right hydronephrosis. Stricture of right ureter. Pyelitis and pyelonephritis	Cystoscopic dilatation of ureters. Kidney pelvis lavage. Prostatic massage. Sounds. Bladder lavage	None	Improved
8 E. G.	12-11-28	41	Frequency, microscopic pyuria, hematuria, pain in left lumbar region and perineum. Impotence	Operated elsewhere for kidney stone ten years ago. Chronic prostatitis with calculi	Calculus in left kidney and multiple shadows of calculi in prostate	None	None	Patient left before treatment was instituted
9 D. M. S.	5- 4-39	57	Pain in right and left lumbar regions. Nocturia, frequency, pain in perineum, urgency, difficulty, dysuria, change in urinary stream. Retention	Adenomatous prostatic hypertrophy with minute prostatic calculi felt by rectum. Pos. cultures. 50 pus cells per H.P.F. Residual 4 oz.	Multiple faint shadows of prostatic calculi. Excretory cystogram revealed considerable residual after urination	Catheter drainage. Massage. Instillations. Sounds and bladder lavage	Perineal prostatectomy for removal of adenomatous gland and multiple calculi	Cured
10 M. V. A.	3-19-35	61	Frequency, burning, rectal symptoms. Prostoscopy negative. Passed bits of gravel, small green stones and concretions on several occasions. Hematuria, pyuria. Positive culture. Bilateral orchi-epididymitis. Retention	Enlarged and boggy prostate by rectum. Difficult catheterization due to stricture of deep urethra. Unable to urinate. At times chills and fever. Prostatic abscess	Multiple seed-like prostatic calculi seen	Drainage of prostatic abscess through urethra by prostatic massage. Sounds, catheters and bladder lavage	Perineal prostatotomy	Cured

TABLE II (*Continued*)

Case No. Name	Date of Exam.	Age	Symptoms	Clinical Findings	Roentgenologic Diagnosis	Urologic Treatment	Surgical Treatment	Results
11 S. B.	11-28-31	60	Hematuria, pyuria, frequency, burning and difficulty. Bladder tenesmus, dysuria and pain in perineum	Enlarged boggy prostate 3 oz. residual cloudy urine. Cystoscopy revealed tumor in diverticulum of urinary bladder	Cystogram revealed retentive type of diverticulum. Filling defect shows presence of bladder tumor. Minute, faint shadows of calculi in area of prostate	Bladder lavages, sounds and prostatic instillations	Partial cystectomy to remove diverticulum containing malignant tumor	Good, for 1 year, from bladder operation. No operation for prostatic calculi. Symptoms persisted but patient left town
12 L. D.	2-27-32	62	Frequency day and night with burning. Pain in rectum and perineum. Prostatic and urinary symptoms for seven years	Prostate enlarged, boggy and leathery, suggesting adenoma and minute seeds of calculi. 40 pus cells per H.P.F. B.P. 170/100. Residual 2½ oz.	Very faint and minute shadows of stones in area of prostate. Cystourethrograms revealed no diverticulum	Bullous edema in prostatic urethra seen at cystoscopy. Multiple cysts at vesical orifice. Contracted vesical neck and median bar	Small stones removed by endoscopic prostatic resection	Improved. Two years later fulguration of cysts of vesical orifice. Still has ½ oz. residual and minor urinary symptoms
13 M. T. M.	4-15-37	56	Frequency day and night, dysuria, difficulty. Urethral discharge on defecation. History of sterility. Heart and prostatic trouble for ten years	Prostate enlarged, boggy, chronically inflamed, adenomatous and full of sand. Residual ½ oz.	Minute, multiple prostatic calculi	Prostatic massage. Deep instillations. Bladder lavage. Sounds and urinary antiseptics	Suprapubic prostatectomy	Cured
14 G. D. P.	12-15-34	30	"Morning drop discharge," dysuria, pyuria and dribbling	Chronic prostatitis. Seminal vesiculitis. 40 pus cells by H.P.F. Urethral stricture	Prostatic calculi. Urethrocystogram revealed prostatic diverticulum with small stone	Prostatic massage. Bladder lavage. Sounds. Kollman dilatation. Deep instillations	Cystoscopic fulguration with removal of stone	Cured
15 J. W. S.	11-18-31	68	Frequency, urgency, burning, dysuria, pyuria, hematuria, pain in perineum. Had operation 30 years ago for rectal fistula. At times severe cystitis with chills and fever. Bladder tenesmus	Prostate enlarged, leathery, adenomatous in type, with small nodule and fluctuation in right lobe. 50 pus cells by H.P.F. Residual urine ½ oz.	Multiple small shadows of calcareous deposits in prostatic area	Bladder lavage. Instillations. Rest in bed. Hot rectal douches. Cathartics. Urinary antiseptics	Prostatolithotomy for removal of calculi and drainage of prostatic abscess	Cured

16 D. S.	7–1–30	46	Frequency day and night, hesitancy and dribbling. Luetic and G.C. history. Persistent urethral discharge. Treatment for prostatitis for many years without cure. Weak sexual power. Difficult erections	Enlarged prostate, boggy, inflamed. Innumerable small concretions of sand felt. 40 pus cells by H.P.F. with clumps. Calcification in the corpus spongiosum of the glans penis	Multiple faint shadows of calculi in the area of the prostate and shadows of calcification in median portion of glans penis	Cystoscopy and urethrocystoscopy negative, except for chronic verumontanitis, inflammation and a few dilated prostatic ducts. Massage, instillations, sounds, dilatations and urinary antiseptics	None	Improved
17 P. L.	6–26–30	37	"Morning drop discharge." Having treatments for G.C. for several years. Has had bilateral orchiepididymitis. Diminished sexual desire. Impotence	Prostate enlarged four times, boggy, inflamed. 50 pus cells per H.P.F. Prostatic calculi not palpable. Chronic prostatitis, and seminal vesiculitis. Bilateral chronic vasitis and small nodule in both epididymites	Multiple, very faint and small shadows of grains of prostatic calculi seen	Has had fulguration of verumontanum elsewhere on two occasions. Prostatic massage. Instillation, Kollman dilatation. Bladder lavage, sounds, urinary antiseptics, *etc.*	None	Improved
18 C. W.	1–5–36	68	Frequency day and night with marked urgency. Dysuria and difficulty. Pain in rectum, perineum and suprapubic region. Patient admitted with complete retention	Enlargement of the prostate with adenoma and sensation of calcification felt by rectal palpation. 36 oz. residual	Small round shadows of calcification in prostatic region	Cystoscopy revealed trilobar adenomatous hypertrophy	Transurethral prostatic resection, 1–10–36. Patient unable to void. Second resection, 1–23–36; about 100 pieces of tissue removed	Good
19 A. D. S.	11–26–35	65	Hematuria, pain in left kidney region, frequency, dysuria, pyuria, burning difficulty. Cystoscopic fulguration of papilloma of bladder neck on two different occasions elsewhere	Rectal palpation suggests small prostatic calculi. Chronically inflamed prostate and seminal vesicles. Tumor mass easily palpable on left side of abdomen	Calcifications in area of left kidney. Evidence of seed-like calculi in region of prostate. Pyelography disclosed left, large-sized renal tumor	Cystoscopy revealed marked bullous edema of vesical orifice. Deep x-ray to inoperable left kidney tumor	None	Unimproved

TABLE II (*Continued*)

Case No. Name	Date of Exam.	Age	Symptoms	Clinical Findings	Roentgenologic Diagnosis	Urologic	Treatment Surgical	Results
20 G. V. K.	7-12-34	60	Frequency with marked dysuria, hesitancy, difficulty, pain in rectum and perineum. Has had prostatic treatment for 20 years without cure	Prostate enlarged and boggy by rectum. Urine loaded with red blood cells and innumerable leukocytes, with clumps. Culture on different occasions shows streptococcus, colon bacillus and staphylococcus	Racemose shadows at the symphysis pubis revealing the presence of multiple prostatic calculi	Cystoscopy revealed bullous edema at floor of vesical orifice. Endoscopic application to posterior urethra. Massage, instillations, bladder lavage. Hot rectal douche. Urinary antiseptics	Refused operation	Fair
21 E. V. F.	5-29-34	76	Frequency day and night. Hazy urine with calcareous deposits and grains of sand voided in the urine on several occasions	Prostate soft in consistency. No stones felt. Cystoscopy revealed much congestion of prostatic urethra with bullous edema at floor of vesical orifice. Occasional leukocytes and red blood cells in urine	Multiple round shadows of prostatic calculi at level of symphysis pubis	Endoscopic applications to deep urethra. Massage, instillations, sounds, bladder lavage	None	Improved
22 F. C.	10-12-38	53	Hematuria, chills and fever, starting in 1908. In 1920, diagnosed bilateral nephrolithiasis. During 1937-1938, profuse hematuria with lumbar pain. High temperature and loss of weight. Received several blood transfusions elsewhere. Frequency, burning, dysuria, pain in perineum	Prostate enlarged, boggy in consistency, containing small calculi by rectal palpation	Bilateral nephrolithiasis in which both kidney pelves are filled with coraliform calculi. Also bilateral ureterolithiasis with good-sized stones in lower portion of both ureters. Evidence of prostatic calculi	Treatment has been medical with urinary antiseptics, blood transfusions, *etc.* No urologic work done	None	Unimproved

23 M. G.	1–9–33	64	Frequency, dysuria, nocturia, difficulty, pain in perineum, chronic constipation. Pain on defecation with watery urethral discharge. Has had G.C. on three occasions	6 oz. residual, cloudy urine. Prostate enlarged, firm and stony in consistency, suggests Ca. and small calcareous deposits in each lateral lobe	Small areas of round shadows of calculi in region of prostate	Cystoscopy revealed congested and swollen bladder neck. Definite hypertrophy of lateral lobes with edema of floor of bladder neck	Perineal prostatectomy for removal of prostatic Ca. and calculi	Cured of calculi for one year
24 H. C.	8–10–35	62	Dysuria, frequency, burning, bladder tenesmus and pyuria	Few tags of infected hemorrhoids present. 4½ oz. residual. Prostate enlarged four times the usual size, adenomatous in type, with hard nodule in posterior lobe, suggesting Ca. Both seminal vesicles distended, and chronically inflamed	Many small shadows of calculi in the area of prostate	Cystoscopy revealed hypertrophy of median lobe with minor hypertrophy of the two lateral lobes	Endoscopic prostatic resection	Improved. Lost sight of after two years
25 E. F.	3–10–37	74	Pain in right lumbar region. Frequency day and night. Pain in rectum and perineum	Small hemorrhoids. Prostate enlarged 1½ times, leathery in consistency. Very small grains of sand or calculi felt. Bilateral hydrocele. Residual 2 oz.	Pyelograms revealed right renal tumor. X-ray disclosed shadows of prostatic calculi in the region of symphysis pubis	Cystoscopy showed slight congestion and bullous edema of floor of bladder neck. Deep x-ray to renal tumor	None	Unimproved
26 L. C.	1–5–37	48	Lumbar sinus eight months after left nephrolithotomy. Frequency, dysuria, pyuria, burning and difficulty. Loss of weight and anemia	Urine is cloudy, contains pus. Prostate enlarged, leathery in consistency, with evidence of small calculi	Left nephrolithiasis with functionless pyonephrotic kidney. Also evidence of small shadows of calculi in area of prostate	Cystoscopy revealed much bullous edema in floor of bladder neck and prostatic urethra	Left nephrectomy. Perineal prostatolithotomy	Cured

TABLE II (*Continued*)

Case No. Name	Date of Exam.	Age	Symptoms	Clinical Findings	Roentgenologic Diagnosis	Urologic	Treatment Surgical	Results
27 A. R.	2-18-36	45	Severe cystitis with blood and pus in urine. Frequency, dysuria, bladder tenesmus. Painful urination, and pain in rectum and perineum	Prostate enlarged and boggy in consistency. Contains minute stones. Patient is acutely ill from severe cystitis. Arthritis and anemia	Plain film revealed three stones in bladder about the size of olives, with many round shadows of phleboliths in bladder and minute shadows of calculi in prostatic region	Bladder irrigations, urinary antiseptics and hot rectal douches	Suprapubic cystotomy for removal of bladder stones. Later perineal prostatolithotomy	Cured
28 W. J. P.	4-9-36	68	Hematuria, dysuria, frequency day and night. Retention and difficulty	Prostate enlarged 2½ times. Boggy, adenomatous in type. 40 pus cells per H.P.F. Residual 4 oz. Minute prostatic calculi felt on rectal palpation	Multiple round shadows of phleboliths, in each side of bladder region. Small round shadows, of prostatic calculi in region of symphysis pubis	Cystoscopy revealed hypertrophy of median and lateral lobes, with multiple cystic degeneration of the mucosa of bladder neck	Endoscopic prostatic resection	Improved
29 F. R. V.	2-20-39	59	Frequency, day and night. Hematuria, tenesmus. Arthritis and hypertension	Microscopic hematuria, and pyuria. Cultures positive for streptococcus and staphylococcus	Multiple round shadows of prostatic calculi in prostatic region	Cystoscopy. Intravenous and retrograde pyelograms	Perineal prostatolithotomy advised. Operation refused	Unimproved

time, to complete the treatment by a perineal prostatotomy for removal of the offending prostatic calculi.

In the diagnosis of prostatic calculi, in addition to the history and the suggestive symptoms, the two most important factors are: First, the clinical findings by rectal palpation of the prostate—revealing the presence of hard nodules and the characteristic sensation of crepitation; and, secondly, the confirmation of the clinical diagnosis by the roentgenologic examination, including both excretory urograms and urethrocystographic studies.

In this series, the presumptive diagnosis was made by rectal palpation in only 67 per cent of cases, and was confirmed roentgenologically in all of them. It was made roentgenologically, however, in 93 per cent, and would undoubtedly have been made in 100 per cent, were it not that in two cases no roentgenograms were taken, because the patients, plainly suffering from prostatic obstruction, were submitted at once to perineal prostatectomy, without preliminary roentgenographic examination, and the minute prostatic calculi were an accidental finding in the specimen removed at operation.

TABLE III

ANALYSIS OF SURGICAL TREATMENT OF 29 CASES OF PROSTATIC CALCULI

Age	Number of Cases	Perineal Prostatolithotomy	Perineal Prostatectomy	Suprapubic Prostatolithotomy	Endoscopic Prostatic Resection	Cystoscopic Fulguration with Endoscopic Removal of Stone	No Operation	Totals
20–29	0	0	0	0	0	0	0	0
30–39	4	0	0	0	0	1	3	4
40–49	6	4	0	0	0	0	2	6
50–59	5	0	1	1	0	0	3	5
60–69	12	2	3	0	4	1	2	12
70–79	2	0	0	0	0	0	2	2
80–89	0	0	0	0	0	0	0	0
Totals	29	6	4	1	4	2	12	29

In Table III, it is seen that the largest group of patients is found in the fourth, fifth and sixth decades. The youngest patient was 30 years of age and the oldest 76. It was a common observation that in individuals over 50 years of age prostatic calculi were found in association with adenomatous prostatic hypertrophy, and, in younger men, in association with prostatitis; furthermore, that in some cases of prostatitis, that were refractory to the usual treatment, prostatic calculi were apparently the underlying cause of the long-standing prostatic infection. In two cases, there was evidence of prostatic abscess, which demanded surgical relief. Two cases exhibited the association of prostatic calculi with carcinoma. One of the latter, operated upon by perineal prostatectomy, lived comfortably for one year following operation, while the other, in whom symptoms of prostatic obstruction were relieved by endoscopic prostatic resection, is known to have lived in fair comfort for at least two years. One patient had a stone in the bladder, which was removed through the cystoscope, while the stones of the prostate were removed later by perineal prostatolithotomy. Another case had a diverticulectomy with partial cystectomy for a malignant growth within the diverticulum. No operation

was performed for the removal of the prostatic calculi, since the patient did not return for further treatments. There have been three cases with a clinical history of having voided small prostatic calculi on several occasions, particularly after prostatic massage. In a few instances, the characteristic click of the metal sound against the stones has been definitely heard. In one case there was definite evidence of association of minute prostatic calculi with calcification of the corpus spongiosum of the glans penis.

Most of the cases in which cultures of the prostatic fluid were made, were positive for several types of organisms, notably the streptococcus, colon bacillus and staphylococcus.

There was practically no case without evidence of 20 to 50 pus cells per high power field in the prostatic fluid, and in most, there was microscopic evidence of pyuria and hematuria in the routine examination of the urinary sediment.

The cystoscopic appearances in some of these patients were most interesting. In some, there was evidence of trilobar prostatic hypertrophy, producing definite obstruction, but it was seldom possible to see the calculi themselves. In one case the small stone was seen impacted in a prostatic diverticulum behind the verumontanum, possibly located in a dilated prostatic duct; this stone was removed by fulguration and endoscopic manipulations. It was striking to observe the presence of marked bullous edema in the floor of the bladder neck and in the region of the prostatic urethra—which appears to be a very constant and characteristic finding in these cases, and helps materially in establishing a correct diagnosis.

TABLE IV

RESULTS OF OPERATIVE TREATMENT IN 29 CASES OF PROSTATIC CALCULI*

	Cured	Improved	Unimproved	Totals
Perineal prostatolithotomy	6	0	0	6
Perineal prostatectomy	4	0	0	4
Suprapubic prostatolithotomy	1	0	0	1
Endoscopic prostatic resection	1	3	0	4
Cystoscopic fulguration	1	1	0	2
No operation	0	5	7	12
Totals	13	9	7	29

* *Summary:* Of 17 cases operated upon, 13 were cured, and four improved.
Of 12 cases not operated upon, seven showed no improvement.

In Table IV are summarized the results of the surgical treatment carried out in 29 cases of prostatic calculi. Of 17 cases operated upon, 13 were cured and four were improved; while of 12 cases that were not operated upon, some of whom were treated with routine urologic measures, five were somewhat improved, and seven showed no improvement.

The type of operation that appears most successful is perineal prostatolithotomy for the removal of the stones. This was performed in six patients, and all were cured. In older men, when the prostatic calculi are associated with adenomatous prostatic hypertrophy, perineal prostatectomy appears to be the procedure of choice. This was performed in four instances, with completely

satisfactory results. Suprapubic prostatolithotomy was also performed in one case, with good result. Cystoscopic fulguration with endoscopic removal of the calculus was performed twice. There were also two cases of recurrence of stone in the prostatic urethra after prostatectomy that were successfully removed by cystoscopic manipulations.

Endoscopic prostatic resection was performed in four cases, and of the four, one was considered cured. The other three were only improved, since all of them still have minor urinary symptoms, and even one to two ounces of residual urine, and the roentgenograms show that there are still multiple seed-like calculi present in the area occupied by the prostate, indicating that the transurethral procedure does not seem to be perfectly adapted to this type of pathologic condition.

Finally, it goes without saying, that every one of these patients who was operated upon was given a complete preliminary preparation for operation, including the repeated P.S.P. tests and blood chemistry, such as is required in a routine surgical case of prostatic obstruction. In fact, some of the cases associated with adenomatous prostatic hypertrophy required an indwelling catheter, and in one instance a preliminary cystostomy for drainage, in order to insure a successful perineal prostatectomy.

CONCLUSIONS

(1) Prostatic calculi are more frequently observed than one might believe from a study of the medical literature. In fact, they are rather a common finding, clinically, operatively and, especially, at autopsy.

(2) Etiologically, prostatic calculi may be classified in three groups: Endogenous—when they are formed in the substance of the gland; exogenous—when, coming from the upper urinary tract, they become deeply imbedded within the region of the prostatic urethra; and mixed or endo-exogenous—when, originating in the prostate, they come in contact with the exogenous elements of the urine which accelerates their growth so that they become in reality prostato-urinary calculi. The intimate interrelationship of these three types of prostatolithiasis may frequently be observed in the same individual.

(3) The most commonly accepted theory of the mode of formation of the minute intraprostatic calculi is that the corpora amylacea in the acini of the gland become surrounded with calcareous deposits, and thus act as nuclei for the development of the true prostatic calculi within the tubules of the prostate.

(4) For purposes of treatment, irrespective of their origin, all classes of prostatic stone, when producing symptoms, demand surgery for their removal.

(5) Asymptomatic stones are not surgical and demand no treatment, but patients in whom they are accidentally discovered should be kept under close observation, since they are harboring a latent infection which may lead to destruction of the parenchyma of the gland, producing obstruction and impairing function, causing abscess and chronic diverticulitis within the gland and even, in advanced cases, complete calcification.

(6) The association of prostatic calculi with parenchymal prostatitis and

adenomatous hypertrophy is a common occurrence. Most of the cases in this series have shown evidence of chronic or acute prostatitis, and, in eight patients, adenomatous prostatic hypertrophy was present.

(7) The symptomatology of this lithiasic disease is insidious. Some cases are asymptomatic, but frequently the patient is suffering from minor urinary, rectal or genital symptoms of an indefinite nature. All the patients in this series had urinary symptoms, ranging from mild frequency and dysuria to total hematuria and complete retention of urine, with all the characteristic symptoms observed as a rule in prostatic obstruction. A few patients complained of urethral stricture. In other instances arthritis or generalized sepsis of long standing was present as the result of prostatolithiasis.

(8) The diagnosis can often be made by rectal palpation of the gland, which in advanced cases elicits a characteristic crepitation and reveals the presence of hard nodules, which can be confirmed by the plain roentgenogram and by urethrocystographic examination.

(9) Cystoscopic examination is helpful in establishing an accurate diagnosis, particularly when there is prostatic hypertrophy or a characteristic bullous edema at the floor of the bladder neck and in the region of the prostatic urethra. It will also serve to determine the best type of operative procedure in each individual case.

(10) The diagnosis was made by rectal palpation in 67 per cent of the cases, and in 100 per cent of cases submitted to roentgenologic examination. No urographic examination should be considered complete without including the region of the prostate, since the discovery of clinically unsuspected prostatic calculi is common.

(11) Of 29 cases herewith reported, 17 came to operation, and, of these, 13 were cured and four improved. Of 12 cases not operated upon but treated medically and urologically, five were improved, and seven showed no improvement.

(12) The paramount surgical consideration is not merely the removal of all prostatic calculi, but is also the maintenance of open drainage, in order to relieve the infection and restore good function, if permanent cure is to be obtained.

(13) The best surgical treatment, when operative intervention is indicated, appears to be perineal prostatolithotomy. When the condition of prostatolithiasis is associated with adenomatous prostatic hypertrophy, perineal prostatectomy assures a permanent cure.

(14) Since the stones as a rule are multiple and in closed infected pockets in cases complicated with prostatitis, or lying near the capsule in cases of adenomatous prostatic hypertrophy, it appears that endoscopic prostatic resection is not applicable in the majority of these cases.

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HYDROCELE OF THE CANAL OF NUCK

REPORT OF SEVENTEEN CASES

VIRGIL S. COUNSELLER, M.D.

DIVISION OF SURGERY, THE MAYO CLINIC

AND

B. MARDEN BLACK, M.D.

FELLOW IN SURGERY, THE MAYO FOUNDATION

ROCHESTER, MINN.

SINCE Coley's[3] comprehensive review of the literature and report of 30 new cases, in 1892, the literature on the subject of hydrocele of the canal of Nuck has been limited mostly to single case reports and the various features of the condition have been neglected. Price,[11] in 1926, expressed the belief that the condition was sufficiently rare to warrant reporting a single case, and he was able to find only eight references in the literature between 1908 and 1926. In the Quarterly Cumulative Index Medicus, since 1926, only three references to it are listed; two are reports of a single case and the third is to an article under the general title, "Hydrocele of Nuck in Japanese Women."

The number of previously reported cases is not large. Wechselmann,[15] in 1890, was able to collect only 62 cases from the literature, and Coley[3] added 30 cases to this list, in 1892. Coley,[4] in 1908, stated that 160 cases of hydrocele of the canal of Nuck had been encountered at the Hospital for Ruptured and Crippled between 1890 and 1908. Since 1892, probably less than 100 cases have been reported. This statement is based on a rather careful search through the "Index-catalogue of the Library of the Surgeon General's Office" and the Index Medicus, and the careful checking of all references available. Several German theses on the subject that have appeared during this period were not available nor were a few reports in more obscure journals. However, we feel that an estimate of less than 350 reported cases is probably not too high. We were unable to find any statistics concerning the incidence of the condition or data relative to the proportion of inguinal herniae complicated by hydrocele among women.

The present communication was undertaken because of the recent lack of interest in the condition, as reflected by references in the literature, and to report the cases encountered at the Mayo Clinic.

Development.—Most writers on the subject are agreed that the cystic tumors which accompany the round ligaments through the inguinal canal of women are the exact counterpart of encysted hydroceles of the cord in the male, and result from the accumulation of fluid in a persisting diverticulum of Nuck, which corresponds to the vaginal process of the peritoneum in the male. In keeping with this conception of origin of the cysts, they are usually

Submitted for publication October 25, 1939.

found accompanying the round ligament but not originating within it, and they are lined with a pavement epithelium similar in all respects to the cells lining the peritoneal cavity. As in the male, the more common form does not communicate with the peritoneal cavity but Coley has reported cases in which such communications exist. In most textbooks essentially the same explanation of the condition is given. Thus Graves[7] considered hydrocele of the vulva to be "a retention cyst due to the upper closure of the processus vaginalis peritonei which runs along the round ligament into the labium majus." Davis[5] stated: "Sometimes a finger-like extension of the peritoneum resembling the vaginal process in the male" accompanies the round ligament through the inguinal canal and the accumulation of fluid in this leads to the formation of the hydrocele.

Other theories to explain the development of these cysts have been proposed in the past. Gebhard[6] suggested that they originated from embryonic rests in the round ligaments, and Weber[14] thought that they could result from the persistence of the original hollow condition of the round ligament. Brothers[1] considered these older theories more completely but they have been largely abandoned at present. It is evident that when a cyst does not have a simple lining of flat cells, it cannot be considered to be an hydrocele and some other explanation for the presence of the epithelial lining must be sought. In most cases reported recently, in which a definite epithelial lining has been found, a cystic adenoma has been present.[10] Further discussion of this point is beyond the scope of this report. However, other cysts than hydroceles do exist in the inguinal canal and in the vicinity of the round ligaments so that microscopic examination of the wall of the cyst is necessary for exact diagnosis.

Classification.—The most common type of hydrocele of the canal of Nuck corresponds to the encysted hydrocele of the cord in the male. There is no communication with the peritoneal cavity and the cyst may be found anywhere along the course of the round ligament from the internal ring to the vulva. Such hydroceles may be multilocular and most of the larger ones have incomplete partitions.

A second type corresponds to the congenital hydrocele of the male with a communication between the hydrocele and the general peritoneal cavity. Two of the cases collected by Coley were of this category without question and several other cases in his series were probably of this type.

Hydroceles of hour-glass type have been found among women also. Halstead and Clark[8] reported a case of a bilocular hydrocele in a Negress, age 42. The constriction was situated at the internal ring where the round ligament entered the lower sac and, in the same region, there was a free communication with the general peritoneal cavity. The upper sac was intra-abdominal but outside of the peritoneum, whereas, the lower sac was in the inguinal canal and simulated an hernia. The lower sac contained several septa and a bean-shaped free body. Halstead and Clark also referred to a similar case reported by Thierhaber,[13] in which there was no communication with the peritoneal cavity, and to a third, reported by Chiari.[2] In both of these cases inflammation

in the intra-abdominal portions of the sac gave symptoms of serious intra-abdominal disease which were interpreted, in both cases, as intestinal obstruction.

The original classification of Regnoli included hydroceles developing in an hernial sac as well as the encysted and diffuse hydroceles of the cord and the congenital type.

Diagnosis.—The chief importance of the condition lies in the differential diagnosis, chiefly from hernia. Coley believed that the diagnosis was possible in most cases and emphasized the characteristic elastic feel of the cyst, along with its position at the subcutaneous inguinal ring. He further pointed out that hydroceles of the canal of Nuck appear first at the subcutaneous inguinal ring and only later reach the vulva. A careful history, therefore, should serve to distinguish hydrocele from vulvovaginal cysts. Others have emphasized the lack of an impulse on coughing and the fact that the supposed hernia cannot be reduced.

In the 17 cases reviewed from the Mayo Clinic, the differential diagnosis between hernia and hydrocele in the female was very difficult. In most of the cases, rather small tumors were so well confined to the inguinal canal that they could not be palpated readily. Many of the hydroceles were associated with hernia and this confused the question of whether the mass could be reduced and whether there was an impulse on coughing. In some cases the cysts were small enough to be freely movable and to be forced toward the subcutaneous inguinal ring when the patient stood or strained. In virtually all such cases the findings indicated to the examiner the presence of a reducible hernia.

In cases in which the hydrocele had extended beyond the subcutaneous inguinal ring toward the vulva, the findings were more diagnostic. Palpation was much facilitated and the mass could be transilluminated. It was also evident that these tumors could not be reduced completely and that they were not incarcerated herniae.

It was often impossible, particularly among obese patients, to place the hydrocele definitely in the region of the subcutaneous inguinal ring rather than over the femoral ring. It was also impossible to distinguish, with complete certainty, small hydroceles from intrinsic tumors of the round ligament, such as fibromata and lipomata.

A clinical diagnosis of hydrocele of the canal of Nuck presents no particular difficulty when the hydrocele is not associated with hernia or when it is large enough to permit transillumination, careful palpation, and the proper determination of its position in relation to the femoral and subcutaneous inguinal rings. In addition, the history of a nontender, irreducible tumor which is slowly increasing in size would make the diagnosis virtually certain. However, smaller hydroceles, particularly those in association with hernia and those in obese patients, probably cannot be differentiated from other tumors in the inguinal and femoral regions.

Data on seventeen cases.—Seventeen cases of hydrocele of the canal of Nuck proved at operation have been encountered at the Mayo Clinic. Although the condition undoubtedly has escaped diagnosis in a few cases, the finding of so few cases of sufficient importance to treat, would indicate the rarity of the condition. The oldest patient in the series was 51 and the youngest, 28 years. The average age at the time of operation was 37. None of the hydroceles had been noted during childhood and the earliest age at which any patient noticed symptoms was 20. Eleven patients had noted tumor in the inguinal region, and the tumor of four others was found on physical examination. The average duration of symptoms was 19 months. The longest time that a mass had been noticed was 16 years; the shortest, two weeks. The duration of the mass, as noticed by the patient, had no relation to its size. Thus the patient who had had the tumor for 16 years had an hydrocele the size of a plum (about 5 cm. in diameter) which had not increased perceptibly in size throughout this time. The largest hydrocele had been noted for 30 months and, during this time, had slowly increased in size. Only one of the 17 patients complained of spontaneous pain and tenderness, while one patient found that wearing a truss caused pain.

For the most part the cysts were small, averaging about 2 to 3 cm. in diameter and their location was such that, in the majority of cases, a diagnosis of inguinal hernia was made. In the 11 cases in which the diagnosis of inguinal hernia was made before operation, an impulse on coughing was thought to have been present, and in all but two the mass was thought to be at least partially reducible. In two cases a diagnosis of femoral hernia was made before operation; only two cases were correctly diagnosed preoperatively; in two cases in which the hydrocele was almost entirely within the abdomen, no preoperative diagnosis was made, the patients having been operated upon for some unrelated condition. In both cases in which a correct preoperative diagnosis was made, the hydroceles were large, extended into the vulva and could be transilluminated.

The frequent association of inguinal herniae with hydroceles in the female has been stressed by several authors previously (Coley, Johnson,[9] and others). This fact was of considerable importance in the past, when the standard treatment for the hydrocele was the injection of some irritant, usually tincture of iodine, into the sac after aspiration of the contents. In our series, seven of the 17 patients had an associated inguinal hernia. In one case, the hydrocele may have occurred in the hernial sac, but in the others both hydrocele and hernia were present. This definite association of hernia with hydrocele in more than one-third of this series of cases, seems to be of considerable importance if any but operative methods are chosen for treatment.

Two of the hydroceles in this series were of the hour-glass type with the larger loculus located within the abdomen. In one of these cases a questionable preoperative diagnosis of femoral hernia was made, while in the other inguinal hernia was thought to have been present. In both cases, rather large extraperitoneal cysts were found, without free communication with the

peritoneal cavity. In neither case was the presence of an intra-abdominal portion of the hydrocele diagnosed before operation. In one case, operative intervention was performed for the supposed inguinal hernia and in the other for leiomyomata of the uterus.

Eight hydrocele sacs of the canal of Nuck were available for microscopic study. Sections from various parts of the walls were made on the freezing microtome and stained with hematoxylin and eosin. In all cases, the hydroceles were lined with a single layer of flattened cells, indistinguishable from the lining cells of the peritoneum. The remainder of the wall was composed of fibrous tissue which was most dense immediately beneath the free surface. The walls varied considerably in thickness and, in the thicker portions, were surprisingly vascular. In two of the smaller cysts with thick walls, bundles of smooth muscle cells independent of the blood vessels were found. The presence of these cells probably can be explained on the basis of the round ligaments, blending into the walls of the hydrocele in this region. In none of the eight cases studied, could the tissue in the lining be interpreted to be cuboidal or columnar epithelium.

Because of the few cases recently reported, a summary of our 17 cases is included (Table I).

TABLE I

SUMMARY OF DATA ON 17 CASES OF HYDROCELE OF THE CANAL OF NUCK

Case	Age	Duration	Size	Side	Hernia	Remarks
1	44 yrs.	2/3 yr.	3x7 cm.	R.	None	Impulse on coughing, reducible mass
2	41 yrs.	5/6 yr.	Lemon-size; inguinal region. Large cyst in iliac fossa	R.	None	Impulse on coughing, reducible mass; hour-glass type of hydrocele
3	46 yrs.	6 wks.	2x3 cm.	L.	None	Extended into labia
4	31 yrs.	*	Large cyst	R.	None	Chiefly intra-abdominal hour-glass type
5	35 yrs.	1/6 yr.	2½ cm.	L.	L. inguinal	Firm; movable in inguinal canal
6	37 yrs.	5 yrs.	Small	R.	R. inguinal	Impulse on coughing, reducible mass
7	51 yrs.	½ yr.	Hickory nut	L.	None	Pain extending down left leg, worse with menses
8	28 yrs.	*	?	L.	L. inguinal	Diagnosis made at operation
9	47 yrs.	*	?	R.	None	Diagnosis made at operation; hydrocele drained from inside of abdomen
10	36 yrs.	16 yrs.	Plum-size	L.	L. inguinal	Truss caused pain
11	30 yrs.	*	?	R.	R. inguinal	Hydrocele of hernial sac
12	40 yrs.	2 wks.	5x3x3 cm.	L.	L. inguinal	Reducible mass; impulse on coughing
13	37 yrs.	*	Small	L.	None	Impulse on coughing; sudden onset of pain; tenderness; mass became irreducible
14	39 yrs.	6 wks.	Egg-size	L.	None	Reducible mass; impulse on coughing; multilocular hydrocele
15	37 yrs.	*	?	R.	None	
16	45 yrs.	7 yrs.	Contained 6 cc. of fluid	L.	Bilateral; inguinal	Left hernia irreducible
17	42 yrs.	2½ yrs.	12x9x3 cm.	L.	None	Extended into labia; many incomplete septa in hydrocele

* Hydrocele found on physical examination or at operation.

SUMMARY AND CONCLUSIONS

The question of the incidence of hydrocele of the canal of Nuck cannot be answered. The small number of reported cases together with the rarity of the diagnosis at the Mayo Clinic is at variance with some previous reports. The diagnosis presents much difficulty, particularly when the hydrocele is confined to the inguinal canal and is too small or is so placed that adequate palpation and transillumination cannot be employed. The finding of an impulse on coughing and the apparent reducibility of the mass cannot be relied on to distinguish hernia from hydrocele in the female. Hernia was associated with hydrocele in seven of the 17 cases in our series. The most important differential diagnostic procedure to distinguish hernia from hydrocele is transillumination. The wall of the hydrocele is made up chiefly of fibrous tissue with a single layer of flattened cells on the inner surface. Smooth muscle may be present in the wall but its finding is not constant.

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BRIEF COMMUNICATIONS AND CASE REPORTS

PARTIAL GASTRIC RESECTION FOR CARCINOMA*

TWO CASE REPORTS OF FIVE-YEAR SURVIVALS

FRANK GLENN, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY OF THE NEW YORK HOSPITAL AND CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK, N. Y.

I WISH to briefly present two patients whom I have treated surgically for gastric carcinoma. The first is that of a man of carcinoma age whose symptoms should have led to a much earlier diagnosis. He was treated by several physicians over a period of 15 months, and was undiagnosed until he was observed to have a prominent epigastric tumor.

The second case was a much younger individual who, for ten years had been under care for a peptic ulcer and who, it is believed, was properly diagnosed within a few weeks of the development of a gastric carcinoma. This early diagnosis, which is so highly desirable in the treatment of gastric carcinoma, was the result of frequent and careful examination.

CASE REPORTS

Case 1.—New York Hospital, No. 47644: J. P. C., male, age 50, was admitted, December 11, 1933, because of indigestion. His symptoms dated back 15 months when he first experienced severe and intractable diarrhea. This persisted for three months and then diminished. It was followed by a six months' period of transient nausea and later occasional vomiting. Six months prior to admission the patient began to vomit almost all the food he ingested. He then became constipated. Roentgenologic examination at that time was said to have been negative. However, because of his symptoms he was told by several physicians that he had a variety of lesions. He was directed, by a friend, to an "Indian" doctor who prescribed a mixture of herbs which relieved the constipation. For two months prior to admission, the patient was able to retain only liquids, he was constantly nauseated, and had a sense of fullness in the epigastrium. From the onset of his symptoms until the patient entered the hospital he had lost between 30 and 35 pounds in weight.

Physical Examination revealed a well-developed but somewhat emaciated individual. The mucous membranes and skin were pale. There was no palpable Virchow's node, and the chest examination was negative. A definite arteriosclerosis was present. Blood pressure 104/74. The abdomen was scaphoid and the superficial veins were prominent. Just above, and to the right of the umbilicus there was a firm, hard, rounded mass, approximately 15 cm. in diameter, which seemed to be connected with a dilated, palpable stomach lying above and to the left of it. The mass was movable and could be dislocated in an orbit of about 20 cm. The liver and spleen were not palpable. Rectal examination was negative.

* Presented before the New York Surgical Society, November 8, 1939. Submitted for publication January 10, 1940.

Laboratory Data.—R. B. C. 4,200,000; Hb. 88 per cent; W. B. C. 11,200. Differential, normal. Urine, negative. Stool examination, repeatedly 4+ for occult blood. Blood Wassermann negative. Gastric analysis: material aspirated was foul-smelling, containing necrotic tissue and blood clots. No free acid was demonstrable. Roentgenologic examination revealed a large, dilated stomach with an obstructive type of peristalsis. There was a huge filling defect with a moth-eaten appearance involving the distal one-third of the stomach (Fig. 1 A). A six-hour examination showed practically complete retention. A 24-hour examination revealed a 75 per cent retention of barium. Doctor Weintraub's impression was carcinoma of the pyloric end of the stomach. A chest roentgenogram showed no evidence of metastasis.

A B

FIG. 1.—Case 1: (A) Roentgenogram taken preoperatively, November 20, 1933. (B) Roentgenogram taken October 30, 1939.

Operation.—December 14, 1933: Ethylene anesthesia. A tumor was found, which measured approximately 12 x 20 cm., involving the distal one-third of the stomach, beginning along the lesser curvature and extending both anteriorly and posteriorly. There were a few enlarged lymph nodes in the mesentery along the lesser curvature. There were no evidences of metastases in the liver, and no free fluid in the abdomen. Between one-third and one-half of the distal portion of the stomach was removed; a Billroth II type of resection being performed. The patient's postoperative course was entirely uneventful.

Pathologic Examination.—Gross: A segment of the stomach showed a large cauliflower mass arising from its lesser curvature. This measured 14 cm. in diameter and projected about 3 cm. above the level of the mucosa. It was composed of papillary, injected, soft masses covered by a yellowish, mucoid secretion. There was a margin of about 3 cm. of normal gastric wall at the cardiac and pyloric portions of the stomach beyond the lesion. There were several large, firm lymph nodes along the lesser curvature. Sections of six of these were taken for microscopic examination. The serous layer of the stomach was smooth and slightly roughened in places, but there was no apparent penetration of the growth into its substance.

Microscopic.—Sections through the tumor showed a profuse growth of neoplastic glandular tissue that extended outward from the mucosa. A very thin connective tissue framework supported large tubular structures made up of columnar epithelium with basally situated nuclei and a clear, unstained cytoplasm. Considerable mucoid material lay in the lumina of these. The growth did not quite extend through the muscular layers. Considerable tissue reaction was evidenced by large numbers of lymphocytes and plasma cells in the submucosa. Sections of six of the regional lymph nodes showed

edema and increase in the retothelial elements, but no evidence of cells of a malignant neoplastic type. Sections through the marginal stomach wall immediately adjacent to the tumor showed considerable inflammation, but no evidence of tumor invasion.

The postoperative course of the patient was uncomplicated, other than for a definite, slowly progressive cerebral arteriosclerosis. The patient has been observed at six-month intervals in the Surgical Follow-Up Department. He has increased in weight from 102 to 133 pounds. The last gastro-intestinal series was made October 30, 1939, and was reported by Doctor Weintraub as revealing a small stomach with a Billroth II operation. The stoma was well placed and functioned normally (Fig. 1 B). There was no evidence of recurrence.

This is an example of a patient of carcinoma age who came to the hospital with a history of gastro-intestinal symptoms of 15 months' duration, which is, in retrospect, almost pathognomonic of carcinoma of the stomach. A partial gastric resection for a palpable tumor was performed. Now, almost six years after operation, he exhibits no evidence of metastases.

Case 2.—New York Hospital, No. 2585: E. P., female, age 37, was admitted to the New York Hospital complaining of epigastric pain. Her history, extending back for ten years, was compatible with duodenal ulcer. She had been seen in 1932 in the Medical Clinic and was found to have epigastric tenderness and roentgenolographic evidence of a duodenal ulcer. She improved on a dietetic ulcer regimen, alkalies and belladonna; sometime later a gastro-intestinal series was reported as being negative. One year prior to admission, the patient had a recurrence of all her symptoms and roentgenologic examination revealed a prepyloric ulcer with a crater (Fig. 2 A). A gastric analysis showed free acid 44; total 60. On rigid treatment she improved, until one month before admission when her symptoms reappeared, and could not be controlled by medical treatment. For a month prior to admission she had vomited practically once a day. No bloody or coffee-ground material was observed in the vomitus. She had lost about 20 pounds in weight.

Physical Examination revealed a thin young woman who showed some evidence of recent loss of weight. The skin and mucous membranes were pale; the lungs clear; blood pressure 140/92. There was slight tenderness in the epigastrium. The remainder of the examination was negative.

Laboratory Data.—R. B. C. 4,400,000; Hb. 80 per cent; W. B. C. 7,900. Differential, normal. Urine, negative. Wassermann, negative. Gastric analysis showed a total acidity of 20, free acidity of 4. Stools, 4+ for occult blood. Roentgenologic examination of the stomach showed an irregular narrowing of the pyloric end of the stomach and a gastric ulcer, with a crater. The findings were interpreted by Doctor Weintraub as those of a carcinoma of the pyloric portion of the stomach.

Operation.—November 23, 1934: An indurated, crater-like ulcer, 2.5 cm. in diameter and 2.0 cm. deep, was found on the posterior wall of the prepyloric region of the stomach. The regional lymph nodes were not apparently involved. In addition, there was scarring, suggesting a healed duodenal ulcer. A Billroth II type of resection was performed, removing one-third of the distal portion of the stomach. The patient's postoperative course was uneventful.

Pathologic Examination.—Gross: The specimen consisted of the distal portion of the stomach. On the posterior aspect of the lesser curvature there was a deep, crater-like ulcer measuring 2.5 cm. in diameter and 2.0 cm. deep. It had a firm, irregular edge with a grayish, dirty coating over the ulcerated surface. At one point in the base of the ulcer, the stomach wall was only 2 Mm. in thickness. There was some puckering and induration externally around the area of the lesion. The remainder of the mucosa appeared normal. There were no enlarged lymph nodes accompanying the specimen.

Microscopic.—Sections from the gastric lesion showed the ulcer to be covered by a

degenerated fibrinopurulent exudate. Beneath this area there was a dense connective tissue with a scattered infiltration of lymphocytes, plasma cells and eosinophils. Throughout this region there were many small groups of large, irregular cells which were rather hyperchromatic, had a large, oval nucleus, prominent nucleolus and frequent mitotic figures. These cells were arranged in small gland-like structures or in groups or cords of two or three. Some normal mucosa was shown on the edge of the section, but this region, likewise, was infiltrated in the deep tissue by cells of similar appearance to those described above.

A B

FIG. 2.—Case 2: (A) Roentgenogram taken preoperatively, November 21, 1934. (B) Roentgenogram taken October 30, 1939.

Postoperatively the patient has been symptom-free. A gastro-intestinal series, October 30, 1939, showed a stomach with the Billroth II operation (Fig. 2 B). Doctor Weintraub reports: "Stoma of the gastro-enterostomy is well placed and functioning normally. There is no evidence of metastasis or recurrence."

This is an example of a patient with a history of ulcer of ten years' duration. A duodenal ulcer was diagnosed, and apparently relieved by treatment. There followed a gastric ulcer which failed to respond to treatment and was proven to be a carcinoma. Five years after operation she shows no evidence of metastases.

DISCUSSION.—DR. GEORGE T. PACK (New York) said that his interest in these two case reports by Doctor Glenn has to do with certain factors in prognosis which they illustrate quite well. Both patients are to be congratulated not only because they came under Doctor Glenn's capable care and survived partial gastrectomy for cancer but, of equal importance, because of the type of cancer which they had, representing the two most favorable varieties or gross anatomic types of cancer of the stomach. In the first, it was a bulky, papillary exophytic tumor growing into the lumen and, although invading the wall, not metastasizing to regional nodes—a tumor which belies its bulk by a relatively slow course and attended by a good prognosis. On microscopic section, it is apparent that it is of low grade malignancy—Grade 1, or Grade 2. The second tumor was an instance of cancer developing on an ulcer in a patient who, until the last few months, at least, had hyperacidity. This patient, also, was without regional metastasis to the nodes. Of course,

these two patients represent successful results of surgery. If one is to be able to present cured patients five years after detection or diagnosis of the cancer is made, a radical procedure such as gastrectomy must be employed.

Palliative operations for gastric cancer are never successful enough to permit the surgeon to present his patients five years after operation, if he employs such procedures as jejunostomy, gastrostomy, simple exploration alone, or plus radiation. The longest duration of life after jejunostomy, in a survey recently made by Doctor Pack, is six months; after gastrostomy 16 months; after simple exploration, plus interstitial radium, 14 months.

One can rest assured that if Doctor Glenn's hospital is comparative to other hospitals in the country, that, at the end of five years, the very best figures will be only 4.5 per cent cures of the total numbers of patients with gastric cancer seen. In other words, for the two patients shown to-night, it may be assumed that there have been 50 who applied to the institution, in the same period, who have died of the disease. His two cases represent the successful end-results in those 50 patients. The statistics collected by Doctors Livingstone and Pack, to which Doctor Pack referred, were collected from the time of Billroth's original report down to January, 1939, representing more than 2,000 references to the world literature.

Of 100 patients coming to the hospital with cancer of the stomach, and seeking cure, 40–80 per cent are immediately incurable, because, at the time they come, they are inoperable. They are not even suitable for celiotomy, even for exploration, or for gastro-enterostomy. The operability rate, therefore, varies from 60 to 20 per cent. Only about 50 out of 100, in the very best hospitals, are suitable to have the abdomen opened. Forty to 60 per cent of these remaining patients are lost as soon as the abdomen is opened, because only palliative operations are found to be possible. Therefore, we have left only a small percentage which, in the average accredited hospital, is only 25 per cent of the 100 patients coming in with gastric cancer. Only one out of four can have a resection—let alone five-year survival. Of those who have the gastric cancer removed, a certain percentage die of the operation, this operative mortality varying from 10 to 60 per cent. The operative mortality is high in some of our best hospitals. If we subtract the operative mortality, the balance represents where cure can begin; this is only 15 or 20 of the original 100 who came in. Following through, then, for the three-, five- and ten-year periods, which are called definitive cures or survival without recurrence, two-thirds are dead in three years, three-fourths in five years, and four-fifths by ten years, and, in the end, very few are left. Doctor Glenn's two patients fall within the group of patients with cancer of the stomach, technically resectable, without metastasis to the lymph nodes, in which Balfour showed 52 per cent survival at the end of five years.

Dr. J. William Hinton (New York) felt that Doctor Pack was rather optimistic, and based his opinion on the fact that, recently, when reviewing over 444 cases of cancer of the stomach, admitted to Bellevue Hospital in 20 years, he had noted two amazing findings. One was that operability does not vary with duration of symptoms. In other words, patients with cancer of the stomach, with symptoms of one month's duration, have no better chance than those with symptoms existing for one year. That, of course, goes back to the question of degree of rapidity of growth of cancer. The other discovery was that the true incidence of resectability of cancer of the stomach is far lower than is generally appreciated. For the physician who sends one favorable case to a special clinic, he has one or two he never sends to anyone, and these cases are never reported. Of the 444 cases admitted to Bellevue in 20

years, approximately 5.5 per cent were resectable. Two-thirds of those seen were inoperable and, of these, 50 per cent died while on the medical ward within a very short period of time after admission.

Dr. Sigmund Mage (New York) summarized the experience to date with radical surgery of carcinoma of the stomach at Mt. Sinai Hospital, and said that it bore out, almost exactly, the statistics presented by Doctor Pack. Only 40 per cent of the cases come to exploration, and only 35 per cent of those explored are found to be resectable. Cases have been followed at Mt. Sinai Hospital since 1922. One hundred thirty-nine resections were performed between 1922 and 1934, inclusive, the period during which there may have been a five-year, or longer, survival. Fifty-three deaths occurred in the 139 radical resections, or an operative mortality of 26 per cent. There were 86 operative survivals. Seventy-nine of these patients have been followed; seven were lost to follow-up. Sixty-five of the 79 died from recurrence of their disease; 61 died within five years. Four lived beyond the five-year period; as follows: One for 79 months; one for 87 months; one for 108 months; and one for 13 years. Three of these latter four cases are known to have died from recurrent carcinoma. Fourteen cases have been followed five years or longer, and of these, 12 remain under observation. Two were lost sight of within the past two years, one having been alive for five years and the other for nine years after operation. At present, one patient is alive 17 years after operation; one, 15 years; one, 14 years; three, ten years; two, nine years; one, seven years; and three, five years after operation. The patient living 17 years, and two of those living ten years after operation had nodular involvement. This group of five-year, or longer, survivals actually represents 17 per cent of the cases who survived radical resection.

As Doctor Pack has brought out, the experience at Mt. Sinai Hospital indicates that of every 100 patients entering Mt. Sinai Hospital to-day with carcinoma of the stomach, 60 will be found to be hopelessly inoperable; 40 will come to operation, and of these 26 will be found to be inoperable and 14 resectable. Of the 14 resectable cases, four will die as a result of the operation. Of the ten survivors, eight will be dead before five years, leaving just two patients of the original 100 with the prospect of living five years or longer.

GUNSHOT WOUND THROUGH THE ABDOMINAL AORTA

CASE REPORT

BORRIS A. KORNBLITH, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF DR. FRANK J. MC GOWAN, GOUVERNEUR HOSPITAL, NEW YORK, N. Y.

REPORT of the appended case seems worthy of record because the patient was still alive nine days after he sustained an apparently fatal wound.

Case Report.—Hosp. No. 41826: J. R., white, male, age 39, was admitted to the Gouverneur Hospital, August 12, 1939, with a history of having been shot, ten minutes previously, while bending over and facing his assailant.

Physical Examination.—The patient was pale, and in moderate shock. Blood pressure 100/65; the pulse ranged between 130 and 140. The wound of entry was found just to the right of the xiphoid cartilage. There was no wound of exit. The entire upper abdomen was held involuntarily rigid. There was no obliteration of liver dulness, and there was no evidence of any intrathoracic injury. The trachea was in the midline. The heart was not shifted. There was no change in the breath sounds. A roentgenogram of the abdomen showed the shadow of the bullet in the region of the second lumbar vertebra just to the left of the midline.

Operation.—An intravenous infusion of 1,000 cc. of 5 per cent glucose in saline was administered preoperatively, and a transfusion of 1,000 cc. of blood was begun at the same time as the exploratory celiotomy was undertaken. The procedure was begun one and one-half hours after the injury had been sustained.

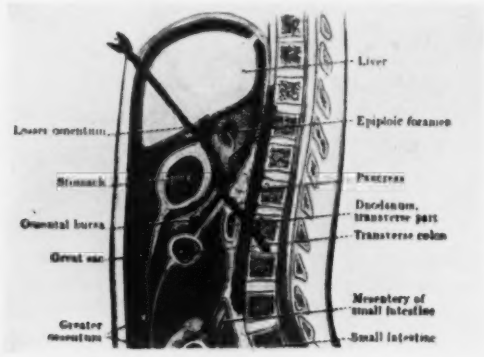
Under gas-oxygen-ether anesthesia a 21-cm. right rectus muscle splitting incision was made. The peritoneal cavity contained about 1,000 cc. of fresh blood but no free air. There was active bleeding from a 4-cm. laceration in the superior surface of the left lobe of the liver. Another laceration, which bled freely, was present on the under surface of the left lobe of the liver. The further course of the bullet was found to be as follows: A small hole was present in the gastrohepatic ligament; another similar hole in the transverse mesocolon—after the bullet had traversed the lesser sac. When the great omentum and transverse colon were reflected cephalad, a small, ½-cm., subserosal hematoma was seen just touching the superior border of the transverse portion of the duodenum as it crossed the aorta. This small tear was closed by a single suture. A very thorough exploration of all the hollow viscera revealed no perforation (Fig. 1 A and B). It was possible to suture both lacerations in the liver and thus control the bleeding. A Penrose drain and one strip of packing were placed to the under surface of the liver. The abdomen was closed in layers. Time of operation was one and one-half hours.

Postoperative Course.—The immediate postoperative condition was good. The pulse became reduced to 110 per minute, and the blood pressure rose to 134/90. Glucose and saline intravenously and additional transfusions were administered during the succeeding days. The temperature ranged between 100° to 102° F. Colonic irrigations controlled the abdominal distention, and a Levin tube was employed repeatedly to relieve gastric retention.

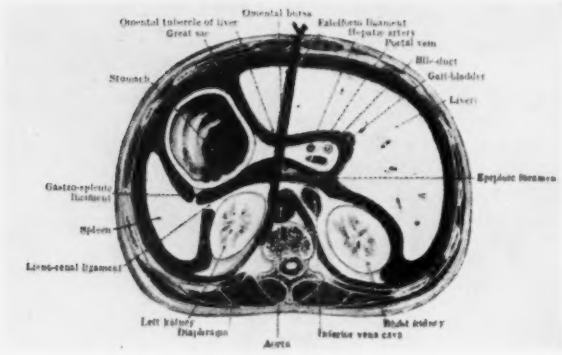
On the fourth postoperative day, he developed a moderate jaundice. Bile was present in the urine. On the fifth postoperative day signs of pulmonary congestion began to appear in both lower lobes. After his general condition had been relatively good for six postoperative days the patient began to lose ground, and died on the ninth day.

Submitted for publication November 27, 1939.

Autopsy.—Path. No. 4734 (Medical Examiner): Dr. B. M. Vance: The sclerae and the skin were jaundiced. The bullet wound of entrance measured 4 Mm. in diameter, with a rather slight zone of abrasion around it. It was located practically in the midline just below the xiphoid cartilage. The bullet passed through the left lobe of the liver at about the middle of its superior surface, and coursed backward before emerging. The bullet holes of entrance and exit had been sutured. There were a number of traumatic infarcts present about the bullet opening. The bullet then passed downward and back-



A



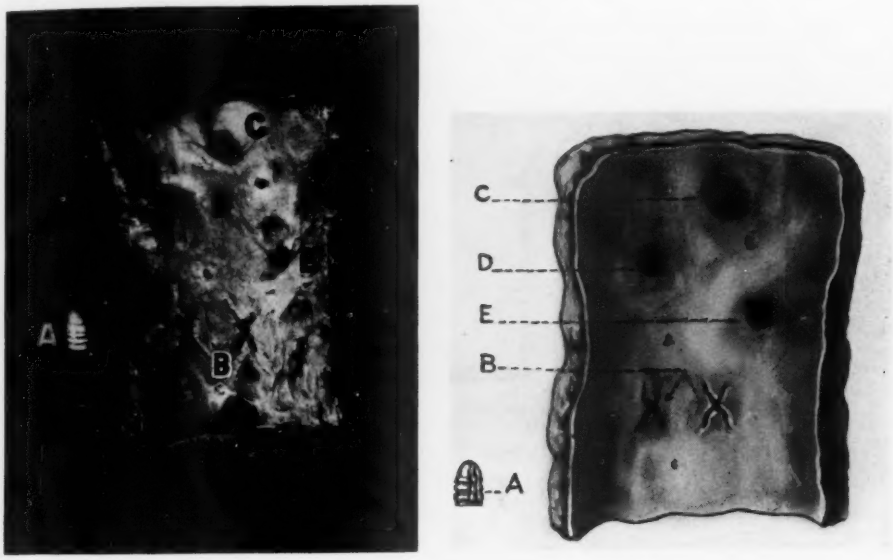
B

FIG. 1.—A and B: Diagrams in sagittal and longitudinal section showing the path of the bullet: Skin at xiphoid cartilage, rectus abdominis, fascia and muscle, parietal peritoneum, superior surface of the liver, left lobe of the liver, gastrohepatic ligament, the lesser sac, transverse mesocolon, superior border of transverse portion of the duodenum, abdominal aorta, and the body of the second lumbar vertebra. (Diagrams from Cunningham's Text-Book of Anatomy, Revised 4th Ed., p. 1235 and 1239, 1916. William Wood and Co., Baltimore.)

ward causing "binocular" openings in the abdominal aorta on its left side. These openings were stellate in shape, and were placed side by side in the same transverse plane about 15 Mm. apart. The lacerations measured 15 Mm. in length and 6 Mm. transversely. The bullet was recovered from the body of the second lumbar vertebra immediately behind the openings described above. The bullet was a .22 caliber, lead one (Fig. 2 A and B). There was a suture coapting a small rent located at the third portion of the duodenum near the jejunum. Except for local reaction about the operative site there was no evidence of peritonitis. Both lungs showed marked edema and hypostatic bronchopneumonia. *Pathologic Diagnosis:* Bullet wound of abdomen, liver, aorta and second lumbar vertebra; hypostatic bronchopneumonia.

Discussion.—In both civil life and during war, gunshot injuries of the aorta have, apparently, been uncommon. The extensive reports of the last war

do not cite any cases which came to operation (Wallace[1]). A search of the literature yielded only two cases that are pertinent. Brentano[2] reports the case of an infantryman who lived for 70 days after a "binocular" gunshot wound through the abdominal aorta near the renal arteries. The soldier, injured during a battle in the Russo-Japanese war, died because of a perito-



A B

FIG. 2.—A and B: Photograph of gross specimen and descriptive drawing of the segment of aorta in the region of the first and second lumbar vertebrae. (A) .22 caliber lead bullet. (B) Gunshot lacerations of the aorta. (C) Superior mesenteric artery. (D) and (E) Renal arteries.

nitis and an infected hematoma in the right lumbar gutter. At a postmortem examination the perforations in the aorta were discovered. A photograph of these perforations is very similar to those shown in Fig 2 A and B of the case herewith reported. The hematoma originated from a laceration of the liver caused by the bullet passing through it. There was no thrombus in the aorta nor any evident bleeding about the site of the perforation in it. Fibrin blocked the efflux of any blood from the vessel. There was no sign of aneurysm formation at the end of 70 days, although Brentano states that he had seen aneurysm formation much earlier resulting from tangential injuries of smaller vessels.

The fact that a through-and-through injury of the aorta tends to close over, is illustrated by the remarkable case of Edmundson.[3] An African native walked into the hospital with a "pulsating" arrow protruding from his anterior chest wall. He had been shot at close range, 13 hours previously. The patient died on the operating table when the point of the arrow was withdrawn from the ascending portion of the aorta. The point of the arrow had transfixed the vessel, but caused no hemorrhage until the attempt at removal was made.

The case reported herewith and the two cited above illustrate that injuries of the aorta with preservation of continuity of the vessel may repair them-

selves and are not necessarily fatal. However, when a large vessel is injured it is generally accompanied by such extensive damage to intervening soft parts in transit that the patient either dies immediately or very soon afterward, as a result of the complicating injuries.

In the present instance, there was no peritonitis or injury to any hollow viscus. The patient died of a complicating hypostatic bronchopneumonia. This pulmonary complication may be attributed to the length of time the exploratory celiotomy consumed, and to the initial shock that the patient suffered. The initial shock, however, may have saved his life for the time being.

The perforation of the aorta in two of the three cases here cited must be classified as "lesions overlooked" since they were not discovered until the postmortem examination. However, according to one series of 164 cases of perforating wounds of the abdomen, reported by McGowan,[4] the lesions overlooked constituted nine per cent, or 15 cases. A thorough exploratory celiotomy is thus apparently of greater importance than speed in completing the operative procedure.

SUMMARY.—(1) A case of bullet wound of the abdomen involving the left lobe of the liver and the abdominal aorta is reported.

(2) The patient lived for nine days, and died of a complicating hypostatic bronchopneumonia.

(3) Two additional cases are cited from the literature.

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Walter Estell Lee, M.D.
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ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa.